

**Volume VI of IX (Appx55385-Appx58360)**  
**No. 2024-1285**

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**UNITED STATES COURT OF APPEALS**  
**FOR THE FEDERAL CIRCUIT**

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APPLE INC.,

*Appellant,*

v.

INTERNATIONAL TRADE COMMISSION,

*Appellee,*

MASIMO CORPORATION, CERCACOR LABORATORIES, INC.,

*Intervenors,*

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On Appeal from the United States International Trade Commission  
in Investigation No. 337-TA-1276

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**NON-CONFIDENTIAL JOINT APPENDIX**

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RDX-8 - Direct Demonstratives of Steven Warren **[SEALED]** Appx70841-  
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RDX-11 - Stephen Scruggs Demonstratives Appx70955-  
Appx70956

### **ADDITIONAL DOCUMENTS**

USPTO Order Denying *Ex Parte* Reexamination for U.S. Patent Appx70957-  
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USPTO Order Denying *Ex Parte* Reexamination for U.S. Patent Appx71011-  
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Remedy or Extend the Target Date and Stay Proceedings Pending Appx71222  
Resolution of Any appeal of the Patent Office's Decision that  
United States Patent Nos. 10,638,941, 10, 595,731 and 9,572,499  
Are Unpatentable (ITC Inv. No. 337-TA-1266)

CX-0635C-MASITC 01076914 - Appendix B - Masimo Watch Appx71223-  
R&D Expenditures, LTD Labor **[SEALED]** Appx71227

CX-0635C-MASITC-01076914 - Appendix B - Masimo Watch Appx71228-  
R&D Expenditures, R&D Summary **[SEALED]** Appx71231

CX-0624C-MASITC-01076803 – Appendix C - Watch Corporate Appx71232-  
Expenditures, v1, v2, v3 **[SEALED]** Appx71233

CX-0632C-MASITC-01076911 - Appendix F - Watch Sourcing Appx71234-  
IT and Recruiting Expenditures, Summary **[SEALED]** Appx71235

CX-0450C-MASITC-01076919 - Appendix M - Masimo Wrist Worn R&D Expenditures, Summary **[SEALED]** Appx71236-Appx71240

CX-0648C-MASITC-01076927 - Appendix S - Watch Headcount, v1 **[SEALED]** Appx71241-Appx71244

Mickle, Tripp, *Apple Keeps Losing Patent Cases. Its Solution: Rewrite the Rules*, N.Y. Times (Mar. 19, 2024) Appx71245-Appx71250

CERTIFICATE OF SERVICE

**CONFIDENTIAL MATERIAL OMITTED**

The material omitted from Appx9; Appx36; Appx41-44; Appx46-48; Appx108; Appx119; Appx121-122; Appx150-151; Appx153-154; Appx156-158; Appx187-190; Appx192-194; Appx196; Appx198; Appx218; Appx220-222; Appx265-276; Appx373; Appx13067-13069; Appx21846; Appx22790; Appx22954; Appx22956-22958; Appx22985; Appx22990; Appx23139; Appx23166; Appx23171-23174; Appx23238; Appx23249; Appx23251-23252; Appx23280-23281; Appx23283-23284; Appx23286-23288; Appx23317-23320; Appx23322-Appx23323; Appx23326; Appx23328; Appx23348; Appx23350-23352; Appx23395-23406; Appx23656; Appx23658; Appx23681-23682; 23688; Appx23791; Appx24147-24148; Appx40795-40798; Appx40996-40999; Appx41019-41026; Appx41029-41030; Appx41058-41062; Appx41077-41080; Appx41094-41097; Appx41108-41110; Appx51900-51924; Appx52602-52606; Appx52609; Appx52642-52645; Appx52791-52795; Appx52822-52824; Appx52911-52912; Appx52939-52941; Appx52980-52982; Appx53016-53019; Appx60425-60431; Appx60432-60434; Appx70322-70355; Appx70774; Appx70781-70783; and Appx70841-70876 contains Apple's confidential competitively sensitive product information subject to the Administrative Protective Order; the material omitted from Appx4579 and Appx53459-53461 contains competitively sensitive information regarding confidential agreements; the material omitted from Appx23439; Appx23441-23446; Appx23448; Appx23450-23453; Appx23455-23458; Appx23462; Appx23617; Appx23621; Appx23659-23665; Appx25251; Appx40483; Appx40582-40584; Appx40600-40601; Appx40605; Appx40652-40655; Appx40658-40662; Appx53491; Appx53492; Appx53497; Appx53499; Appx53503; Appx53506; Appx65064-65075; Appx65075; Appx65104-65105; Appx65315; Appx65321-65232; and Appx71223-71244 contains Masimo's confidential competitively sensitive financial information subject to the Administrative Protective Order; the material omitted from Appx311-316; Appx23667-23674; Appx40579-40581; Appx40585-40599; Appx40602-40604; Appx40610-40614; and Appx40631-40633 contains Masimo's confidential competitively sensitive financial and manufacturing information subject to the Administrative Protective Order; the material omitted from Appx473-474; Appx62; and Appx23176-23178 contains Masimo's confidential competitively sensitive manufacturing information subject to the Administrative Protective Order; the material omitted from Appx13047; Appx14129-14140; Appx205-206; Appx211; Appx21848; Appx22282-22286; Appx23197; Appx23204; Appx23335-23336; Appx23341; Appx23408-23416; Appx23434-23436; Appx23454; Appx23642; Appx23644-23645; Appx23647-23649; Appx23685-23687; Appx23693-23697; Appx23704; Appx25253-25260; Appx278-286; Appx2809-



2852; Appx2923-2937; Appx304-306; Appx309; Appx3708; Appx3710-3711; Appx3718; Appx3722; Appx3725; Appx3727; Appx3732; Appx3733; Appx3735; Appx40229-40232; Appx40346-40371; Appx40407-40422; Appx40431-40434; Appx40438-40442; Appx40486-40494; Appx40495-40506; Appx40512-40521; Appx40525-40528; Appx40547-40555; Appx40560-40574; Appx40803-40822; Appx41217-41221; Appx41350-41356; Appx53070-53095; Appx53107-53151; Appx53222-53234; Appx53236-53252; Appx53256-53361; Appx53362-53365; Appx53813-53838; Appx53927-53941; Appx54064-54226; Appx54227-54266; Appx55229-55354; Appx55359-55376; Appx55386-55399; Appx57317-57324; Appx57394--57409; Appx57410-57412; Appx57615-57618; Appx60136-60153; Appx60184-60212; Appx65014-65019; Appx65022-65025; Appx65028-65037; Appx65040-65074; Appx65207; Appx65224; Appx65267-65268; Appx67; Appx6701-6703; Appx6705; Appx6732-6736; Appx6852-6854; Appx6937-6950; Appx70475; Appx70484-70491; Appx70504-70513; Appx70518-70559; Appx70610-70613; Appx70615-70617; Appx70619-70628; Appx70833-70835; Appx70948-70950; Appx70955-70956; and Appx74 contains Masimo's confidential competitively sensitive product information subject to the Administrative Protective Order; the material omitted from Appx23707-23709; Appx318; Appx320-328; Appx40634; and Appx70592-70594 contains Masimo's confidential competitively sensitive product and financial information subject to the Administrative Protective Order; the material omitted from Appx176; Appx179; Appx22788-22789; and Appx22791 contains Masimo's confidential information detailing non-public patent prosecution subject to the Administrative Protective Order; the material omitted from Appx404-405; Appx457; Appx460-461; Appx464; Appx24103-24104; Appx25387; and Appx25389 contains Apple's confidential competitively sensitive financial and sales information subject to the Administrative Protective Order; the material omitted from Appx52602-52608 contains confidential competitively sensitive product of a third party.

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Until now no fingertip pulse oximeter has been available with Masimo SET® Measure-through Motion and Low Perfusion™ pulse oximetry – the same technology used on more than 100 million patients a year in leading hospitals worldwide.

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**Stig Severinsen**  
Ph.D. in medicine, four-time World Champion freediver and owner of multiple Guinness World Records, including history's longest breath-hold of 22 minutes



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4/28/2021

Apple Watch Series 6 review: minute improvements - The Verge

CX-1608

APPLE

# APPLE WATCH SERIES 6 REVIEW: MINUTE IMPROVEMENTS

*The watch is great, the blood oxygen monitor is not*

By Dieter Bohn | @backlon | Oct 1, 2020, 10:00am EDT

Photography by Vjeran Pavic / The Verge

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W

eirdly, the fact that the Apple Watch Series 6 is the very best smartwatch by a huge margin feels anticlimactic. That's probably because the same was true of the Series 5, the Series 4, and even the Series 3. At this point, the company would have to massively screw something up with the Apple Watch for it to be knocked out of the lead spot.

Apple didn't screw anything up. But that's not the same thing as significantly moving forward, either. The Series 6's updates comprise a bunch of very minor updates that will be unnecessary to the vast majority of people who will buy it. The headline feature, blood oxygen monitoring, also fits in that category.

Starting at \$399, it's not the best deal you can find for your wrist, but it justifies its cost by offering a ton of value — just not enough value compared to previous generations that you'd notice it. It's an iterative update, in other words.

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VERGE SCORE

## APPLE WATCH SERIES 6

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#### GOOD STUFF

- Big, bright display
- Solid ecosystem of third-party complications
- Built-in sleep tracking

#### BAD STUFF

- Still no third-party watch faces
- Still no Android phone support
- Blood oxygen monitoring is unreliable.

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*The Apple Watch Series 6 maintains compatibility with all the same watch straps.*

## APPLE WATCH SERIES 6: HARDWARE UPDATES



ther than the fact that there are new color options like red and blue, it's virtually impossible to distinguish the Series 6 from its predecessor. The only tell is that the sensor array on the bottom is different to accommodate the blood oxygen sensor on the newer watch. It's still a lozenge-shaped square with a big, beautiful screen and it still offers an array of finishes in two sizes, 44mm and 40mm.

The Series 6 has slightly faster charging — in my tests it was charging from zero to 100 percent in a little over two hours, while the Series 5 hit 80 percent. That's a fairly minor bump, but it is marginally useful since more people will be looking to charge it at in-between times so they can take advantage of the new sleep tracking features in watchOS 7.

**THE SERIES 6 IS PHYSICALLY INDISTINGUISHABLE FROM THE LAST GENERATION**

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*A new Apple Watch watch face.*

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*The buttons are unchanged on the Apple Watch Series 6.*

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*The sensor array on the bottom is different because of the new blood oxygen monitor.*

There's a new processor inside the Series 6, but that hasn't affected my experience at all — battery life and speed both appear to be identical to last year's model. That means I'm getting about a day and a half (including sleep) on a single charge, but less if I use it for exercise tracking.

The always-on standby screen is brighter than on the Series 5, but I never really had a huge problem with brightness on the older model. Finally, there's an always-on altimeter and the aforementioned blood oxygen sensor.

Add all those iterations up and I believe that if you have a Series 5 or Series 4, there's not a compelling reason to upgrade. This many generations in, it's clear that the upgrade cycle for the Apple Watch ought to be closer to three or five years for most people.

If it is time for you to get an Apple Watch — either your first one or as an upgrade — a harder question for me to answer is *which* one to get. There's the Series 6 and there's also the new Apple Watch SE, which lacks an always-on screen but otherwise supports



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the vast majority of things most people want out of a smartwatch. The low-cost Series 3 is still sticking around, and heck, if you can find a refurbished Series 5 or 4 I think either of those would be a good buy.

Trying to parse the differences between the different Apple Watch models is about as difficult as trying to distinguish the dozens of slightly different phones Samsung makes. Instead of offering clear choices based on features, Apple is flooding the zone with an option at every conceivable price point from \$200 on up to well over a thousand bucks.

My honest advice is to spend as much as you're comfortable with, and don't sweat that you're missing something vital by ignoring the upsell. Because the truth is that the things that make the Apple Watch Series 6 great are shared by all those other Apple Watches.



*There's a new "artist" watch face.*

## WATCHOS 7

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If you haven't looked into the third-party app ecosystem for the Apple Watch in awhile, I bring you good news: it's great now. There are third-party apps for many of the things I want on my watch, including bike ride tracking, trail maps, Google Maps, and more detailed weather apps.

I don't usually get to these apps via the Apple Watch's app list, though, I usually launch them via watch face complications. Apps can now put more than one on a single watch face, which offers just a bit more customization. I still can't find a single watch face I like to use all the time, but the new options do make it easier for me to set activity-based faces to switch between. I have a work face, a weekend face, a biking face, and a cooking face.

The watch face I use for cooking, Count Up, is nice because it has a built-in stopwatch in addition to the main stopwatch app. Of course, it's only necessary because Siri still can't set multiple timers.

The Apple Watch now does native sleep tracking, but I might end up sticking with a third-party app for that. Apple's system is built in, but it pushes you into using Apple's wind-down bedtime feature. I find its bedtime reminders restrictive and sometimes even patronizing — it's worse than my parents were when I was eight and stayed up too late reading with a flashlight. Anyway, watchOS 7's sleep tracking reports are also less detailed than what you can get from a third-party app or even from another smartwatch like the Withings HR.

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Sleep Schedule

Multiple

[Show More Sleep Data](#)

## Your Schedule

Next



Summary



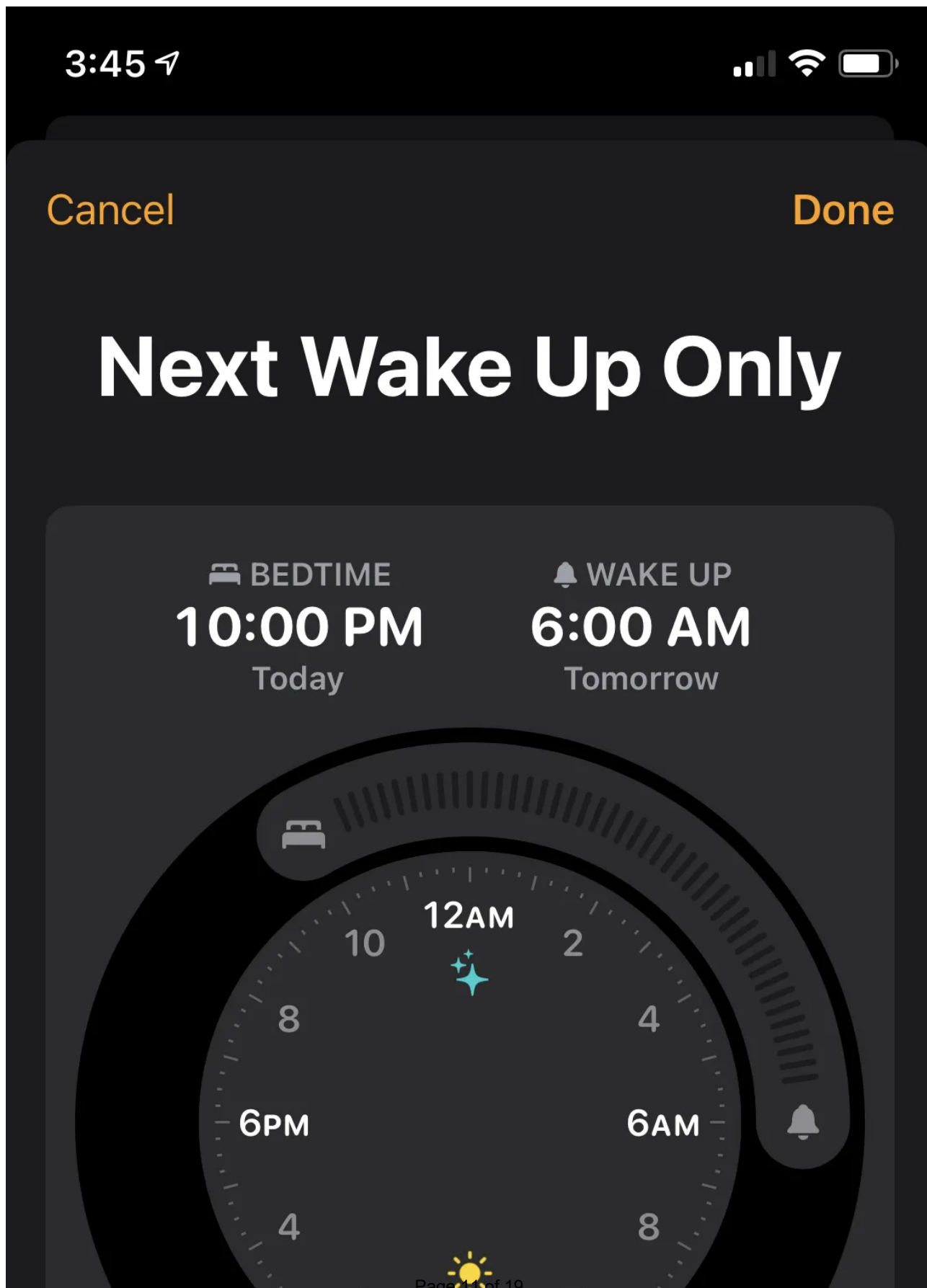
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*The new sleep tracking feature doesn't provide a ton of data.*

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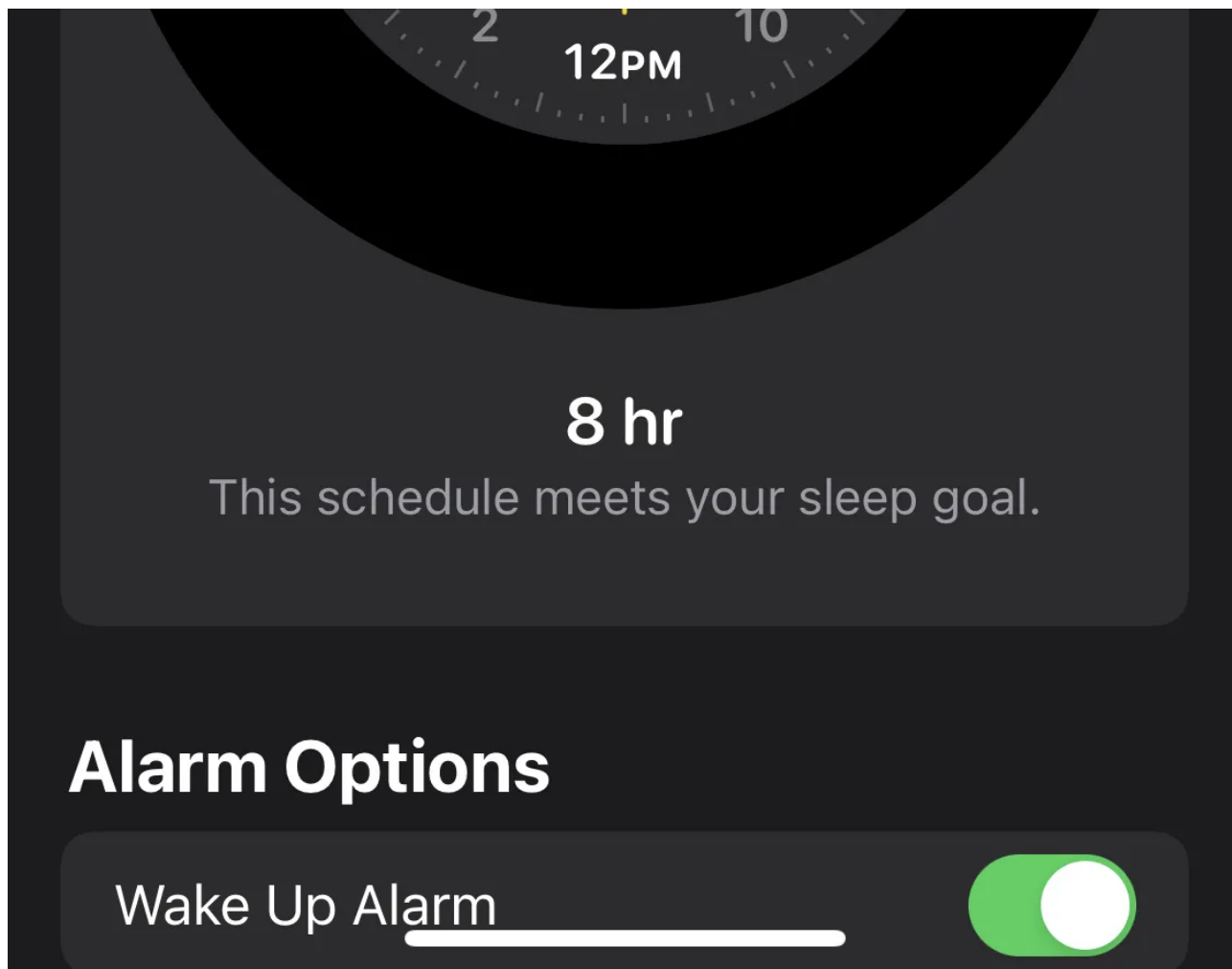


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*Apple has a new bedtime feature that works, but is restrictive when it comes to DND options.*

Later this year, Apple will release its Fitness Plus service that integrates with the Apple Watch by displaying your health stats on top of workout videos. I wasn't able to test that, but I'll be interested to give it a try when it releases. I did use Apple's new biking directions fairly extensively and found them really helpful — but I'm also lucky enough to live in an area where they're available.

The most intriguing new feature in watchOS 7 is Family Setup, which lets you set up a cellular Apple Watch for a kid or parent as a managed device. My colleague Dan Seifert has been testing it and will have much more to say about it in another review. Here, I'll just note that Dan tells me that unless you spend a lot of time configuring stuff as a parent, you're effectively handing a full Apple Watch with all its features and complexities to a child, which seems like a lot to me.

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And I know it's about as effective as howling at the moon, but I do wish Apple would find a way to make the Apple Watch available for Android users — even if it's only by making it even more independently useful.



*The blood oxygen monitor often can't get a reading.*

## BLOOD OXYGEN TRACKING

I have been covering gadgets for a very long time now and in that time I've built up a strong aversion to gimmicky health gadgets. Every time I go to the Consumer Electronics Show I am beset with small companies making vague claims that their wellness devices will do something vital for my health — and those claims wilt under the slightest inquiry about scientific rigor, academic studies, or FDA clearances.

I've never associated the Apple Watch with those digital snake oil gadgets because Apple has historically been responsible about its claims and features. For the blood oxygen monitor, Apple is not making any specious claims. But because the results it

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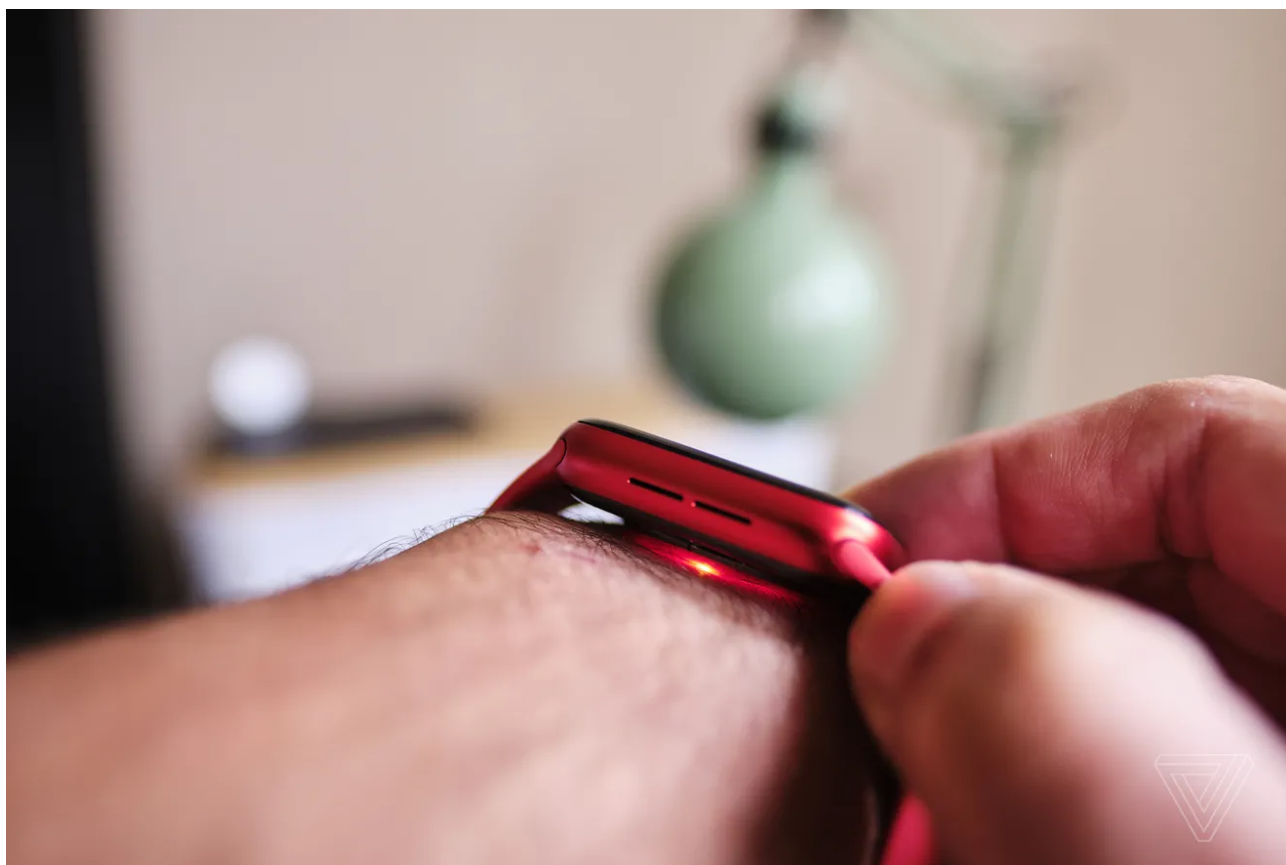
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provides require so much context and are unclear so often, I trust this blood oxygen monitor way less than I trust the other sensors on the watch.

The system works in one of two ways. First, you can measure your blood oxygen manually. To do so, you need to rest your arm on a horizontal surface for 15 seconds while it takes a reading. More importantly, though, you have to make sure the watch is quite snug and correctly placed on your wrist. It needs to be positioned a ways up your arm — quite a bit higher than how I usually wear a watch.

***IF YOU DON'T FOLLOW THE INSTRUCTIONS EXACTLY, YOU LIKELY WON'T GET A READING. AND WHEN YOU DO, THE RESULTS ARE STILL INCONSISTENT.***



*The blood oxygen monitor's light is quite bright, so much so that you can turn it off when you're in theater mode.*



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*The blood oxygen animation.*

If you follow the directions to a T, you'll usually get a reading. Sometimes you won't, though, and for me that happened much more often than I was expecting. A blood oxygen level over 95 percent is generally considered okay and anything under that may be a sign of a problem. Generally, when I tested the Apple Watch against a finger monitor, the finger monitor gave me a higher reading.

The other way the monitor works is that it tries to read your blood oxygen in the background while you are going about your day or sleeping. Here, I often got numbers that were lower than I expected — I think often because the watch wasn't positioned correctly for an accurate reading.

Other reviewers have run into similar issues. [Joanna Stern at the Wall Street Journal](#) and [Geoffrey Fowler at the Washington Post](#) both reported unreliable results. In a statement to the WSJ, Apple says:

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“The Blood Oxygen feature has been rigorously tested across a wide spectrum of users and across all skin tones. For a small percentage of users, various factors may make it difficult to get a blood oxygen measurement including motion, watch placement on the wrist, skin temperature and skin perfusion.”

Apple also says that this blood oxygen monitor is a “wellness” feature, that it’s not meant for medical diagnostics, and that it isn’t seeking any sort of FDA clearance for it. It won’t be used to send you alerts of troubling results like the heart rate monitor can.

And to be ultra clear: this is not a COVID-19 detector or early warning system. Apple is taking part in studies to see if the sensors on wearables can do something to help with early detection, but those results won’t come in for some time.

Several other smartwatches have blood oxygen monitors, and it may be that trying to measure blood oxygen from your wrist is just inherently problematic. Nicole Wetsman [just reviewed the Withings Scanwatch](#) and found its results to be consistently wrong. (Withings is awaiting a sign-off from the FDA before it distributes it in the US.)

I’m just not sure who Apple intends to use this feature. If you happen to be a high-altitude endurance runner who’s super into quantified self statistics, I think you’ll find a use for it. If you’re not that person, I am not sure that you’ll get anything useful from this sensor.

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*The Apple Watch Series 6, in Product Red.*



Despite my reservations with the blood oxygen detection, the Apple Watch Series 6 is the best smartwatch for the iPhone. The inconsistent results I (and others) got measuring blood oxygen levels don't take away from what makes the Apple Watch great in the first place.

It has very good fitness and health tracking, and Apple's Health app keeps that information secure and private unless you purposefully share it. It integrates so well with the iPhone that it puts other smartwatches at a disadvantage — but that still means it has great support for iMessage, phone calls, Apple Music, and the rest. And for simple, basic smartwatch features like notifications and useful watch faces, watchOS 7 is second to none.

### ***A SMALL UPGRADE, BUT STILL THE BEST SMARTWATCH***

That's all true for the Apple Watch Series 6. But it's also true for any other modern Apple Watch. The second best smartwatch for iPhone users is the Apple Watch Series 5,

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<https://www.theverge.com/21496141/apple-watch-series-6-review-blood-oxygen-monitor-watchos-7>

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followed closely by the Apple Watch SE and then the Apple Watch 3.

I can't help but think that putting the Apple Watch into a yearly release cadence may not be strictly necessary anymore. Apple may keep making these small updates, but that doesn't mean you need to keep up with them. If you have an older Apple Watch that's still serving you in good stead, keep using it. ■

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## AGREE TO CONTINUE: APPLE WATCH SERIES 6

*Every smart device now requires you to agree to a series of terms and conditions before you can use it — contracts that no one actually reads. It's impossible for us to read and analyze every single one of these agreements. But we started counting exactly how many times you have to hit "agree" to use devices when we review them since these are agreements most people don't read and definitely can't negotiate.*

- Since the Apple Watch only works with the iPhone, you will already have consented to two mandatory agreements and (if you use Apple Pay), six optional ones.
- There is a terms and conditions agreement specifically for watchOS, which you can have emailed to you. Apple is transparent that many of the privacy settings you've chosen for your phone will transfer over to the Watch.

These agreements are mandatory, and you cannot negotiate them.

There are several more optional agreements:

- If you transfer your Apple Pay cards to work on the Watch, you may have to agree to additional terms from your bank. In my case, Bank of America includes a location sharing provision and provides a link (which you have to manually type out yourself) to a [PDF with more information](#).
- If you set up cellular, you might have to agree to more terms from your carrier, but we couldn't test every one. Verizon, at least, didn't ask me to agree to additional terms, although it did ask for a \$30 activation fee.

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- If you want to use blood oxygen monitoring, you must turn on location so that Apple can verify you live in an supported area. Similarly, emergency fall detection also will share your location whether or not you have it enabled in settings.

Final tally: one mandatory agreement, at least three optional agreements, and all the agreements necessary to use an iPhone.

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**The Washington Post** *Democracy Dies in Darkness*

# The new Apple Watch says my lungs may be sick. Or perfect. It can't decide.

Both the Apple Watch Series 6 and Fitbit Sense have new blood-oxygen apps. They're mostly useless.

By Geoffrey A. Fowler

Columnist

September 23, 2020



Sometimes the new Apple Watch Series 6 reports my lungs and heart are the picture of health, pumping blood that's 100 percent saturated with oxygen.

At other times, it reports my blood oxygen is so low I might be suffering from emphysema. (I am not.)

The watch can't decide. This much is clear: Don't buy one of these \$400 devices in the hopes of monitoring your lung health.

An Apple oxygen check a day will not keep the doctor away, at least not yet. The way consumer tech companies are marketing health capabilities is getting ahead of what their gadgets can actually, reliably do. That's a dangerous trend, and it jeopardizes the potential positive effect that collecting body data could have on our health.

It's particularly deceptive at a time when many people are looking to health monitors for any clue that they may have covid-19, the illness caused by the novel coronavirus.

For the past week, I've been wearing a smartwatch on each wrist, all day and all night long. On the right I have the Apple Watch Series 6, and on the left I wear the new \$330 Fitbit Sense, which went on sale this week.

There are many reasons people buy wearable gadgets. I wear an Apple Watch for fitness motivation and to receive phone notifications, and an

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Oura Ring to track my sleep. But this fall's smartwatch upgrades from Apple and Fitbit are all about health. Apple's slogan reads: "The future of health is on your wrist."

These watches also read heart rate and rhythm, but I'm focusing this review on the headline addition to the Apple watch and the Fitbit: an oximeter, which measures the oxygen in your blood. Doctors are increasingly treating oxygenation as a vital sign (alongside pulse and temperature) because it can help reveal aspects of conditions including sleep apnea, pulmonary embolism and covid-19. That certainly sounds helpful to have on your wrist.

That's what Apple Vice President for Health Sumbul Ahmad Desai implied at Apple's prerecorded launch event. "Adding blood oxygen brings another valuable health measurement to users. Blood oxygen and pulse oximetry are terms that we've heard a lot about during the covid pandemic," she said.

But you start to get a different picture when you read what both companies say in their disclaimers. Neither device is approved by the Food and Drug Administration.

The tiny type at the bottom of Apple's website says its blood oxygen app is "not intended for medical use" and is "only designed for general fitness and wellness purposes." Fitbit's small print says its blood-oxygen app is "not intended to diagnose or treat any medical condition" and is useful to "help you manage your well-being and keep track of your information."

There are important differences in the blood oxygen data that Apple and Fitbit report. But in my experience, neither company's measurement serves much purpose at all. You should know what you're buying, because it might do more harm than good.

## Measuring blood: Finger vs. wrist

To understand my frustrating Apple Watch readings, I called pulmonologists who haven't had a chance to test the watches but understand the science. When doctors test blood oxygen, they often use sensors on fingers called pulse oximeters. These devices shine light through the skin and nail to detect the color of the blood as a measure of how much oxygen is there. They produce a measure called SpO<sub>2</sub>; most healthy people range between 95 percent and 100 percent.

The finger oximeters used by doctors are approved by the Food and Drug Administration. To compare my smartwatch results, I bought a finger oximeter for \$60 from Medline Industries that is FDA approved and

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reports an error rate of plus or minus two percentage points.

Unlike finger pulse oximeters, these two smartwatches try to read your blood oxygen from your wrist. And they're conspicuously silent about accuracy.

Apple's new watch has lights on the bottom to generate signals that are reflected back from the blood in your wrist and read by sensors. An app lets you do spot checks anytime and also runs on its own while you sleep. You have to hold really, really still for 15 seconds to get a reading.

The first time I tried this on the Apple Watch 6, it said my oxygen level was 88 percent — shockingly low, given that I am in good health and wasn't wheezing. Five minutes later, I tested again and it said my SpO<sub>2</sub> was 95 percent. I kept trying it and kept getting different readings — and, frequently, an “unsuccessful measurement” error message.

I told Apple about my experience, and it sent me a new watch. My first measurement on my second Apple Watch 6 reported my SpO<sub>2</sub> as 100 percent. If these readings were accurate, my lungs were having a really wild Wednesday.

Over several days of comparing my second Apple Watch's measurements to my FDA-approved finger oximeter, Apple's readings most often differ by two or three percentage points — though they've also sometimes exactly matched, and sometimes have been as much as seven percentage points lower.

Is it just me? Skin, fat and blood vessels do vary. Apple would not comment on the error rate of its sensor, but spokeswoman Amy Bessette said it “has been rigorously tested across a wide spectrum of users and across all skin tones.” (When I tested the Apple Watch on a colleague whose skin is darker than mine, the results were also off from the finger pulse oximeter, but less wildly so.)

Bessette also said, “For a small percentage of users, various factors may make it difficult to get a blood oxygen measurement including motion, watch placement on the wrist, skin temperature and skin perfusion, and the blood oxygen app provides dynamic feedback to help users get the best reading possible.”

The company sent me additional Apple watch straps — eight in total — to wear while testing its second watch. This year, Apple is selling a new kind of stretchy band that is called the Solo Loop and comes in a variety of sizes. Going down one size (to a model that leaves a slight imprint on my wrist) did eliminate some but not all of the “unsuccessful measurement” error messages.

With the Fitbit, I've had less-erratic results, but the device also provides a lot less information. You can't ask the Sense to run spot checks. Instead, it measures your SpO<sub>2</sub> while you sleep and provides a nightly average.

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My oxygen level, Fitbit reports, is typically in the range of 95 percent to 97 percent. That sounds believable, though I can't compare it to results from my finger pulse oximeter because I'm not awake to turn it on.

In an interview, Fitbit's director of research, Conor Heneghan, said the company decided the overnight view was a more reliable piece of information. "It's a pretty hard technical problem to measure SpO<sub>2</sub> on the wrist," he said. Unlike fingers, which have many blood vessels near the surface that offer a strong signal, the wrist is prone to obstructions and poor readings.

"You move a little bit, or even just you are a little bit colder than normal, you can get a very weak signal," Heneghan said. "We've gone after long-term averaging, so that way, when we take overnight measurements, we can comfortably exclude the periods when we feel that signal is too noisy or weak to be reliable."

Heneghan still wouldn't disclose the Fitbit's exact error rate. But he said it beats the range set by an international standards organization. That's not much to brag about: It would allow someone with a true SpO<sub>2</sub> reading of 95 percent to be told they're at 91 percent.

He was forthcoming on the testing Fitbit did, such as working with a lab at the University of California at San Francisco to test the device on volunteers, including people with different skin tones. "We tried to overrepresent darker-skin-toned people in our testing to make sure that it's not skewed toward a particular tone," he said.

## Marketing vs. medicine

Let's be clear: These companies are marketing a device with medical functions while winking and insisting they're not medical functions. Okay, so then what else, exactly, are we supposed to use oxygen apps for?

Fitness? You can't use these sensors while you work out. Just the slightest bit of movement — even breathing too heavily — sends my Apple Watch into error mode. Neither Apple nor Fitbit makes any effort to explain how your SpO<sub>2</sub> levels might be linked to your workouts. (SpO<sub>2</sub> is different from another oxygen indicator called VO<sub>2</sub> Max, which measures how your body uses oxygen while you exercise.)

That leaves us with the industry's term "wellness." So, are we supposed to get together with friends over drinks and talk about O<sub>2</sub> stats? "Hey, bud, my hemoglobin works better than yours!"

Whatever the fine print might say, some people are going to treat these as medical devices — and that's a concern

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HEALTH CARE — AND THAT'S A CONCERN.

“Pulse oximeters can tell you in a trending situation if your oxygen is in the normal range,” said Albert Rizzo, the chief medical officer for the American Lung Association. But it’s not necessarily a leading indicator of problems, including covid-19. “Nobody should be waiting for their pulse-ox to go down before calling their doctor,” he said.

There could be consequences if consumers actually believe the hype about these devices. “I agree with you that it is a dangerous trend for technology companies to release medical devices that don’t meet FDA standards and claim that they are not medical devices,” said Brian Clark, a pulmonologist and professor at the Yale University School of Medicine.

The most common negative consequence is likely to be people calling their doctors too often because of false low readings. “But the more concerning and potentially dangerous scenario is when the devices provide false reassurance and people don’t seek health care when they really need it,” Clark said.

Apple was more upfront in 2018 when it added an electrocardiogram, or ECG, app to its watch. It did get FDA clearance (not quite the same as “approval”) for its app, and worked with researchers to publish studies on its accuracy. But still, there’s fine print: the Apple Watch’s irregular-rhythm notification is not intended for use by “those who have been previously diagnosed with atrial fibrillation (AFib).”

Fitbit said an ECG app it added to the Sense this year also received FDA clearance. Why not do the same for the oximeter? “If we were to make a claim, like we could detect sleep apnea, we would definitely go through the regulatory process and be very clear on our messaging and very clear on the limitations,” said Fitbit’s Heneghan.

A release-with-disclaimers approach could leave consumers without guardrails as more body sensors come to market. To the Sense, Fitbit also added a skin temperature sensor and an electrodermal activity sensor — similar to what’s in a polygraph — that it says “may indicate your body’s response to stress.” Neither of those sensors has been cleared by the FDA.

Questions about accuracy also interfere with the work of academics combing through the body data from smartwatches to see if it can be used to detect disease. This summer, I wrote about promising early results from academics using heart rate and temperature data from the Oura Ring and Fitbit to predict the onset of covid-19 symptoms.

Several of those researchers told me they were excited by the addition of blood-oxygen data — but there’s not enough information about its validity.

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“We have toys, and we have things that are used for clinical purposes. And it really needs to be a clear distinction,” said Duke University’s Jessilyn Dunn, an assistant professor of biomedical engineering who is helping to lead a study called Covidentify.

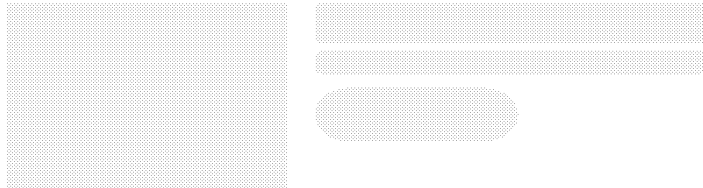
It should not be acceptable for giant tech companies to market devices that take readings of our bodies without disclosing how those devices were tested and what their error ranges might be.

I believe collecting accurate data about our bodies can help advance our health. But the key word here is “accurate.”

By Geoffrey Fowler

Geoffrey A. Fowler is The Washington Post’s technology columnist based in San Francisco. He joined The Post in 2017 after 16 years with the Wall Street Journal. He won the 2020 Gerald Loeb Award for commentary.

 Twitter



CX-1621



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/534,827	08/03/2009	Jeroen Poeze	CERCA.002A	1308

20995	7590	01/16/2015
KNOBBE MARTENS OLSON & BEAR LLP		
2040 MAIN STREET		
FOURTEENTH FLOOR		
IRVINE, CA 92614		

EXAMINER	
LIU, CHU CHUAN	

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
01/16/2015	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jayna.cartee@knobbe.com  
 efiling@knobbe.com

<b>Notice of Abandonment</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	12/534,827	POEZE ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	CHU CHUAN (JJ) LIU	3777

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

This application is abandoned in view of:

1. ☒ Applicant's failure to timely file a proper reply to the Office letter mailed on 20 June 2014.
  - (a) ☐ A reply was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply (including a total extension of time of \_\_\_\_\_ month(s)) which expired on \_\_\_\_\_.
  - (b) ☒ A proposed reply was received on 25 June 2014, but it does not constitute a proper reply under 37 CFR 1.113 to the final rejection.  
 (A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) if this is utility or plant application, a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. Note that RCEs are not permitted in design applications.)
  - (c) ☐ A reply was received on \_\_\_\_\_ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).
  - (d) ☐ No reply has been received.
2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
  - (a) ☐ The issue fee and publication fee, if applicable, was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
  - (b) ☐ The submitted fee of \$\_\_\_\_\_ is insufficient. A balance of \$\_\_\_\_\_ is due.  
 The issue fee required by 37 CFR 1.18 is \$\_\_\_\_\_. The publication fee, if required by 37 CFR 1.18(d), is \$\_\_\_\_\_.
  - (c) ☐ The issue fee and publication fee, if applicable, has not been received.
3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
  - (a) ☐ Proposed corrected drawings were received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply.
  - (b) ☐ No corrected drawings have been received.
4. ☐ The letter of express abandonment which is signed by the attorney or agent of record or other party authorized under 37 CFR 1.33(b). See 37 CFR 1.138(b).
5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34) upon the filing of a continuing application.
6. ☐ The decision by the Board of Patent Appeals and Interference rendered on \_\_\_\_\_ and because the period for seeking court review of the decision has expired and there are no allowed claims.
7. ☒ The reason(s) below:  
  
 An IDS was filed on 06/25/2014, but it does not constitute a proper reply as indicated above.

/TSE CHEN/ Supervisory Patent Examiner, Art Unit 3777	/CHU CHUAN (JJ) LIU/ Examiner, Art Unit 3777
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Petitions to revive under 37 CFR 1.137, or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534,827
	Filing Date	August 3, 2009
	First Named Inventor	Poeze et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 1 OF 4	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	4,684,245	08/04/1987	Goldring	
	2	5,222,495	06/29/1993	Clarke et al.	
	3	5,851,178	12/22/1998	Aronow	
	4	6,325,761	12/04/2001	Jay	
	5	6,668,185	12/23/2003	Toida	
	6	6,681,133	01/20/2004	Chaiken et al.	
	7	6,912,413	06/28/2005	Rantala et al.	
	8	7,047,054	05/16/2006	Benni	
	9	7,092,757	08/15/2006	Larson et al.	
	10	7,365,923	04/29/2008	Hargis et al.	
	11	7,395,189	07/01/2008	Qing et al.	
	12	7,809,418	10/05/2010	Xu	
	13	7,899,506	03/01/2011	Xu et al.	
	14	8,044,998	10/25/2011	Heenan	
	15	8,126,531	02/28/2012	Crowley	
	16	8,219,170	07/10/2012	Hausmann et al.	
	17	8,233,955	07/31/2012	Al-Ali et al.	
	18	8,244,325	08/14/2012	Al-Ali et al.	
	19	8,255,026	08/28/2012	Al-Ali	
	20	8,255,027	08/28/2012	Al-Ali et al.	
	21	8,255,028	08/28/2012	Al-Ali et al.	
	22	8,260,577	09/04/2012	Weber et al.	
	23	8,265,723	09/11/2012	McHale et al.	
	24	8,274,360	09/25/2012	Sampath et al.	
	25	8,301,217	10/30/2012	Al-Ali et al.	
	26	8,310,336	11/13/2012	Muhsin et al.	
	27	8,315,683	11/20/2012	Al-Ali et al.	
	28	8,332,006	12/11/2012	Naganuma et al.	
	29	8,337,403	12/25/2012	Al-Ali et al.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534,827
	Filing Date	August 3, 2009
	First Named Inventor	Poeze et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 2 OF 4	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	30	8,346,330	01/01/2013	Lamego	
	31	8,353,842	01/15/2013	Al-Ali et al.	
	32	8,355,766	01/15/2013	MacNeish, III et al.	
	33	8,359,080	01/22/2013	Diab et al.	
	34	8,364,223	01/29/2013	Al-Ali et al.	
	35	8,364,226	01/29/2013	Diab et al.	
	36	8,374,665	02/12/2013	Lamego	
	37	8,380,272	02/19/2013	Barrett et al.	
	38	8,385,995	02/26/2013	Al-ali et al.	
	39	8,385,996	02/26/2013	Smith et al.	
	40	8,388,353	03/05/2013	Kiani et la.	
	41	8,399,822	03/19/2013	Al-Ali	
	42	8,401,602	03/19/2013	Kiani	
	43	8,405,608	03/26/2013	Al-Ali et al.	
	44	8,414,499	04/09/2013	Al-Ali et al.	
	45	8,418,524	04/16/2013	Al-Ali	
	46	8,421,022	04/16/2013	Rozenfeld	
	47	8,423,106	04/16/2013	Lamego et al.	
	48	8,428,674	04/23/2013	Duffy et al.	
	49	8,428,967	04/23/2013	Olsen et al.	
	50	8,430,817	04/30/2013	Al-Ali et al.	
	51	8,455,290	06/04/2013	Siskavich	
	52	8,457,703	06/04/2013	Al-Ali	
	53	8,457,707	06/04/2013	Kiani	
	54	8,463,349	06/11/2013	Diab et al.	
	55	8,466,286	06/18/2013	Bellot et al.	
	56	8,471,713	06/25/2013	Poeze et al.	
	57	8,473,020	06/25/2013	Kiani et al.	
	58	8,483,787	07/09/2013	Al-Ali et al.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534,827
	Filing Date	August 3, 2009
	First Named Inventor	Poeze et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 3 OF 4	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	59	8,489,364	07/16/2013	Weber et al.	
	60	8,498,684	07/30/2013	Weber et al.	
	61	8,509,867	08/13/2013	Workman et al.	
	62	8,523,781	09/03/2013	Al-Ali	
	63	8,529,301	09/10/2013	Al-Ali et al.	
	64	8,532,727	09/10/2013	Ali et al.	
	65	8,532,728	09/10/2013	Diab et al.	
	66	8,547,209	10/01/2013	Kiani et al.	
	67	8,548,548	10/01/2013	Al-Ali	
	68	8,548,550	10/01/2013	Al-Ali et al.	
	69	8,560,032	10/15/2013	Al-Ali et al.	
	70	8,560,034	10/15/2013	Diab et al.	
	71	8,602,971	12/10/2013	Farr	
	72	8,630,691 (CERCA.003A)	01/14/2014	Lamego et al.	
	73	8,688,183 (CERCA.008A)	04/01/2014	Bruinsma et al.	
	74	2002/0039272	04/04/2002	Abdul-Hafiz et al.	
	75	2006/0220881	10/05/2006	Al-Ali et al.	
	76	2011/0004082 (CERCA.002C1)	01/06/2011	Poeze et al.	
	77	2013/0317370 (CERCA.007C1)	11/28/2013	Dalvi et al.	
	78	2014/0066783 (CERCA.006C1)	03/06/2014	Kiani et al.	
	79	2014/0155712 (CERCA.003D1)	06/05/2014	Lamego et al.	
	80	D692,145	10/22/2013	Al-Ali et al.	
	81	RE43,860	12/11/2012	Parker	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534,827
	Filing Date	August 3, 2009
	First Named Inventor	Poeze et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 4 OF 4	Attorney Docket No.	CERCA.002A

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	82	KANUKURTHY et al., "Data Acquisition Unit for an Implantable Multi-Channel Optical Glucose Sensor", Electro/Information Technology Conference, Chicago, IL, USA, May 17-20, 2007, pp. 1-6	
	83	SMITH, "The Pursuit of Noninvasive Glucose: 'Hunting the Deceitful Turkey'", 2006	
	84	SMALL et al., "Data Handling Issues for Near-Infrared Glucose Measurements", <a href="http://www.ieee.org/organizations/pubs/newsletters/leos/apr98/datahandling.htm">http://www.ieee.org/organizations/pubs/newsletters/leos/apr98/datahandling.htm</a> , accessed 11/27/2007	

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<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

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Electronic Patent Application Fee Transmittal				
<b>Application Number:</b>	12534827			
<b>Filing Date:</b>	03-Aug-2009			
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze			
<b>Filer:</b>	Scott Cromar/Daniella Kellogg			
<b>Attorney Docket Number:</b>	CERCA.002A			
Filed as Large Entity				
<b>Utility under 35 USC 111(a) Filing Fees</b>				
<b>Description</b>	<b>Fee Code</b>	<b>Quantity</b>	<b>Amount</b>	<b>Sub-Total in USD(\$)</b>
<b>Basic Filing:</b>				
<b>Pages:</b>				
<b>Claims:</b>				
<b>Miscellaneous-Filing:</b>				
<b>Petition:</b>				
<b>Patent-Appeals-and-Interference:</b>				
<b>Post-Allowance-and-Post-Issuance:</b>				
<b>Extension-of-Time:</b>				

CX-1621

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
<b>Miscellaneous:</b>				
Submission- Information Disclosure Stmt	1806	1	180	180
<b>Total in USD (\$)</b>				<b>180</b>

CX-1621

<b>Electronic Acknowledgement Receipt</b>	
<b>EFS ID:</b>	19413030
<b>Application Number:</b>	12534827
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	1308
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	20995
<b>Filer:</b>	Scott Cromar/Daniella Kellogg
<b>Filer Authorized By:</b>	Scott Cromar
<b>Attorney Docket Number:</b>	CERCA.002A
<b>Receipt Date:</b>	25-JUN-2014
<b>Filing Date:</b>	03-AUG-2009
<b>Time Stamp:</b>	18:55:01
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$180
RAM confirmation Number	7580
Deposit Account	111410
Authorized User	KNOBBE MARTENS OLSON AND BEAR
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)</p>	

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**Appx57673**

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File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		IDS_CERCA-002A.pdf	66744	yes	5
			b00789b94f453b6c6d08018462403d758bbfced5		
	Multipart Description/PDF files in .zip description				
	Document Description		Start		End
	Transmittal Letter		1		1
	Information Disclosure Statement (IDS) Form (SB08)		2		5
Warnings:					
Information:					
2	Non Patent Literature	KANUKURTHY.PDF	969914	no	6
			a0c0f6391583c384d9025a3d7168ac210032bfa6		
Warnings:					
Information:					
3	Non Patent Literature	SMALL.PDF	267787	no	4
			9b4b481caa1ff259f6aca9f8b51a063774f73a15		
Warnings:					
Information:					
4	Non Patent Literature	SMITH.PDF	6827361	no	129
			fc184af57f5233cc1c56a8d53992bdad22d94c69		
Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	30495	no	2
			e53238e6be210aedd29d5757490b8a4dc43774b7		
Warnings:					
Information:					
Total Files Size (in bytes):			8162301		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



Docket No.: CERCA.002A

Customer No. 20995

**INFORMATION DISCLOSURE STATEMENT**

Inventor	:	Jeroen Poeze
App. No.	:	12/534,827
Filed	:	August 3, 2009
For	:	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
Examiner	:	Liu, Chu Chuan
Art Unit	:	3777
Conf. No.	:	1308

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**References and Listing**

Submitted herewith in the above-identified application is an Information Disclosure Statement listing references for consideration. Copies of any listed foreign and non-patent literature references are being submitted.

**Timing of Disclosure**

This Information Disclosure Statement is being filed after receipt of a First Office Action, but before the mailing date of a Final Action and before the mailing date of a Notice of Allowance. This Statement is accompanied by the fees set forth in 37 C.F.R. 1.17(p). The Commissioner is hereby authorized to charge any additional fees which may be required or to credit any overpayment to Account No. 11-1410.

Respectfully submitted,  
KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: June 25, 2014

By: /Scott Cromar/ \_\_\_\_\_  
Scott A. Cromar  
Registration No. 65,066  
Attorney of Record  
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18292692

CX-1621



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/534,827	08/03/2009	Jeroen Poeze	CERCA.002A	1308

20995	7590	06/20/2014
KNOBBE MARTENS OLSON & BEAR LLP		
2040 MAIN STREET		
FOURTEENTH FLOOR		
IRVINE, CA 92614		

EXAMINER	
LIU, CHU CHUAN	

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
06/20/2014	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jayna.cartee@knobbe.com  
 efiling@knobbe.com

CX-1621

<b>Office Action Summary</b>	<b>Application No.</b> 12/534,827	<b>Applicant(s)</b> POEZE ET AL.	
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777	<b>AIA (First Inventor to File) Status</b> No

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 06/05/2014.  
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on \_\_\_\_.

2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims\***

5) ☒ Claim(s) 1-21 and 23-35 is/are pending in the application.  
5a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.

6) ☐ Claim(s) \_\_\_\_ is/are allowed.

7) ☒ Claim(s) 1-21 and 23-35 is/are rejected.

8) ☐ Claim(s) \_\_\_\_ is/are objected to.

9) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

\* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see [http://www.uspto.gov/patents/init\\_events/pph/index.jsp](http://www.uspto.gov/patents/init_events/pph/index.jsp) or send an inquiry to [PPHfeedback@uspto.gov](mailto:PPHfeedback@uspto.gov).

**Application Papers**

10) ☐ The specification is objected to by the Examiner.

11) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

**Priority under 35 U.S.C. § 119**

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

**Certified copies:**

a) ☐ All    b) ☐ Some\*\*    c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)  
Paper No(s)/Mail Date \_\_\_\_.

3) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.

4) ☐ Other: \_\_\_\_.

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### **DETAILED ACTION**

1. The present application is being examined under the pre-AIA first to invent provisions.
2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/05/2014 has been entered.
3. Claims 1-21 and 23-35 are pending for examination. Claims 22 and 36-44 are cancelled.

### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

(a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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5. Claims 1-21 and 23-35 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for pre-AIA the inventor(s), at the time the application was filed, had possession of the claimed invention. In regard to independent claims 1, 8 and 29, claims 1, 8 and 29 recite "... two or more photodiodes each having characteristics different from one another ... achieve a desired signal-to-noise ratio and accounting for the characteristics of the two or more photodiodes". The specification provides supports such as "combinations of various photodiodes from different manufacturers... were tested as possible embodiments" (paragraph [0275]); Fig. 15J and paragraph [0282] indicates the relationships between SNR and the configurations of 1-4 PD per stream; different configurations of multiple photodiodes coupled to a transimpedance amplifier(s). There is no sufficient support for all possible different characteristics of the photodiodes and accounting for the all possible characteristics of the photodiodes. Second, Fig. 15J illustrates SNR vs. 1-4 PD per stream but does not specify the curves for multiple PDs per stream included various photodiodes from different manufacturers. The specification (paragraph [0275]) discloses combinations of various photodiodes from different manufacturers, different impedance values with the transimpedance amplifier, and different numbers of photodiodes **were tested** as possible embodiments but no results are provided. There is no sufficient evidence(s) to support "the

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transimpedance amplifier is impedance matched to the two or more photodiodes in order to accounting for the *all possible* characteristics of the two or more photodiodes”.

All dependent claims are rejected to as having the same deficiencies as the claims they depend from.

6. The following is a quotation of 35 U.S.C. 112(b):

(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 23-28 and 35 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention. The term "substantially" in claim 23-28 and 35 is a relative term which renders the claim indefinite. The term " substantially " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what the degree(s)/ configuration(s) of substantially linear geometry, equal spacing, unequal spacing, logarithmic spacing, progressive spacing, and / or grid geometry.

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***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-2, 6-13, 15, 19-21, 23-24, 28-31, and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen et al (USPN 5,676,143 - cited in previous action) in view of Wilcken et al. (USPGPUB 2006/0076473- cited in previous action). In regard to claims 1, 8, and 29, Simonsen discloses a noninvasive, physiological sensor and a method capable of outputting a signal responsive to a blood analyte present in a monitored patient (Figs. 13-15, 17-18, and 20), said sensor comprising: a sensor housing (Figs. 13-15 and 17-18); an optical source coupled to said housing (elements 27, 29 and 35, Fig. 13; elements 27 and 59, Fig. 17), said optical source configured to transmit a sequence of optical radiation a tissue site of a patient when said housing is applied to the patient (Figs. 13-15 and 17-18) and to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm at tissue of a measurement site (Col 5 lines 1-62); and a plurality of photo-detecting sites (Figs. 15 and 19), said plurality of photo-detecting sites arranged in a spatial geometry that provides variation in path lengths between at least some of the photodetectors from-and the optical source (Figs. 15 and 19; Figs. 7-12), each of said plurality of photo-detecting sites comprising: two or more optical fibers each configured to detect the sequence of optical radiation from said optical source after attenuation by tissue of said tissue site

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(Figs. 15 and 19 and associated descriptions), each of said two or more optical fibers configured to produce a respective optical signal stream responsive to said detected sequence of optical radiation (Figs. 15, 19, and 20); and an amplifier coupled to the two or more optical fibers (Col 18 lines 29-55 and Fig. 20), the amplifier configured to amplify the optical signal streams transmitted by the two or more optical fibers, wherein each of said plurality of optical fibers is configured to output a detection signal responsive to one or more of the signal streams produced by each photodetector's respective single amplifier (Fig. 20; Note that the same detection rows of optical fibers are respectively connected to one of the photodiodes 70a-70c in order to obtain optical information from the same optical path lengths), and wherein said detection signals are usable to determine a blood analyte based at least in part on the variation in path lengths (abstract and Col 9 lines 4-23). Simonsen does not specifically disclose the use of a plurality of photodetectors at each photo-detecting sites and each of said plurality of photodetectors comprises two or more photodiodes. It is well known in the art that using a photodiode(s) to detect optical signal is equivalent to using an optical fiber(s) to guide the detected light to a photodiode(s) as evidenced by Tsuchiya (Figs. 9A and 9B of USPN 5,441,054 - cited in previous action). Using photodiodes at each detecting rows/sites is equivalent to detect optical signals from optical fibers located in each of the detecting rows/ sites (Figs. 15, 19 and 20) which is connected to an amplifier. Furthermore, Simonsen also discloses the use of a detector array to provide electrical signals in each of the detecting rows (Fig. 7 and associated descriptions). It is also known in the art that a row/ column of the array detector can be connected to a



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transimpedance amplifier in order to obtain detected optical signal(s) as evidenced by Wyles et al. (Fig. 1a of USPN 5,043,820 - cited in previous action). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the detecting configuration of fibers with a detector array to yield predictable results. Simonsen as modified does not specifically disclose a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes, wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio. Wilcken teaches two alternative configurations (Figs. 4 and 5), wherein one configuration comprises a single transimpedance amplifier coupled to the two or more photodiodes having characteristics different from one another (It is known that when manufacturing the same type/ model of photodiodes, there is certain degree of manufacturing tolerance(s) or acceptable variance(s) in each photodiodes. Therefore, even the same type/ model of photodiode would have different characteristics), the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes (elements 410 and 514, Fig. 5 and [0030]), wherein the transimpedance amplifier is impedance matched to the two or more photodiodes (impedance matching element comprised in TIA 512, [0030] and Fig. 5) and accounting for the characteristics of the two or more photodiodes (feedback, controlling gain, and impedance matching or line balancing element, [0030]). It is well known in that art that impedance matching can reduce noise of the signal as evidenced by Seetharaman et

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al. (USPGPUB 2004/0119542 - cited in previous action) and therefore changes the SNR. It would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the array detecting configuration (Simonsen as modified) with the single transimpedance amplifier and signal summing/ impedance matching configurations (Wilcken) in order to obtain the optimal data representing the detected optical signal(s).

In regard to claims 2 and 33-34, Simonsen as modified by Wilcken discloses the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm; at least one pulse at a wavelength of approximately 1650 to approximately 1800 nm; at least one pulse at a wavelength of approximately 900 to approximately 1300 nm (Col 5 lines 1-62 of Simonsen).

In regard to claims 6-7, Simonsen as modified by Wilcken discloses a patient monitor capable of processing the plurality of combined and amplified signal streams to determine output values for one or more physiological parameters (glucose, abstract; Fig. 20 of Simonsen).

In regard to claims 9, Simonsen as modified by Wilcken discloses the blood analyte comprises glucose, wherein the sensor comprises electronic circuitry configured to receive said signals responsive to said detected sequence of optical radiation and wherein said output signal is indicative of said glucose (Fig. 20 and associated descriptions of Simonsen).

In regard to claim 10, Simonsen as modified by Wilcken discloses all the claimed limitations except a display coupled to the sensor housing and configured to display

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information indicating the blood analyte. Simonsen discloses a microcomputer unit (element 74, Fig. 20 of Simonsen) configured to calculate the concentration of blood analyte (abstract of Simonsen). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the sensor to be coupled to a display in order to output/ show the calculation results to the user.

In regard to claim 11, Simonsen as modified by Wilcken discloses a signal medium that is configured to connect to a processing device (Fig. 20 of Simonsen).

In regard to claim 12, Simonsen as modified by Wilcken discloses an interface configured to provide the signal to a device external to the sensor (Fig. 20 of Simonsen).

In regard to claim 13, Simonsen as modified by Wilcken discloses the interface comprises at least one transimpedance amplifier configured to amplify the signal stream from the photodetectors (Fig. 20 of Simonsen).

In regard to claim 15, Simonsen as modified by Wilcken discloses the housing comprises a shell constructed of material capable of reflecting at least some of the optical radiation back into the tissue site (aluminum 53, Fig. 17 of Simonsen).

In regard to claim 19, Simonsen as modified by Wilcken discloses the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site (Col 18, lines 40-49 of Simonsen).

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In regard to claim 20, Simonsen as modified by Wilcken discloses an optical noise reducer capable of reducing ambient light from entering the tissue site (elements 31a and 31b, Fig. 13 and col 18, lines 56-64 of Simonsen).

In regard to claim 21, Simonsen as modified by Wilcken discloses a heat sink configured to dissipate heat from the sensor (aluminum 53, Fig. 17 and Col 19, lines 30-37 of Simonsen).

In regard to claim 23, Simonsen as modified by Wilcken discloses the special geometry comprises a substantially linear geometry (Figs. 7-12 and 15 of Simonsen).

In regard to claim 24, Simonsen as modified by Wilcken discloses the special substantially linear geometry comprises substantially equal spacing (Fig. 10 of Simonsen).

In regard to claim 28, Simonsen as modified by Wilcken discloses the special geometry comprises a substantially grid geometry (Fig. 12 of Simonsen).

In regard to claims 30-31, claims 30-31 encompass the similar scope of the invention as that of the claims 8-9. Therefore, claims 29-31 are rejected on the same ground as the claims 8-9.

In regard to claim 35, claim 35 encompasses the similar scope of the invention as that of the claims 23- 24. Therefore, claim 35 is rejected on the same ground as the claim 23-24.

10. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Simonsen and Wilcken as applied to claim 1 above, and further in view

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of Clarke et al. (USPN 5,222,496 - cited in previous action). In regard to claims 3-5, Simonsen as modified by Wilcken discloses all the claimed limitation except the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm; at three wavelengths about 30 nm apart; and at about 1610 nm, about 1645 nm, and about 1665 nm. Clarke teaches to emit three wavelengths of optical radiation between about 1600 to about 1700 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40); at three wavelengths about 30 nm apart (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; and closely spaced wavelengths will be less than about 30nm wide, abstract and Col 3 lines 9-12); and at about 1610 nm, about 1645 nm, and about 1665 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; 1600nm +/- 15nm, abstract; and about 60nm or 30nm wide, Col 3 lines 9-12) for detecting glucose concentration (Col 3 lines 28-40). The wavelengths taught by Clarke are suitable for measuring glucose concentration. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the wavelengths (Simonsen as modified by Wilcken) with the wavelengths (Clarke) to yield predictable results.

11. Claim 14 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Simonsen and Wilcken as applied to claim 8 above, and further in view of Shaw et al. (USPN 4,114,604 – cited in previous action). In regard to claim 14, Simonsen discloses all the claimed limitations except the interface comprises at least one switched capacitor circuit configured to convert said signal stream from the

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photodetectors into digital information. Shaw teaches at least one switched capacitor circuit configured to convert said signal stream from the photodetectors into digital information (element 17, Fig. 1 and Col 4 line 62 – Col 5 line 8). Simonsen discloses amplifiers (elements 71a-c and 72a-c) for converting the detected signals into digital signals. Shaw teaches using the operationally connected capacitor which compensates for amplifier drift and spurious outputs from the detector (Col 5 lines 1-8). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the interface (Simonsen) to incorporate the switched capacitor circuit (Shaw) in order to obtain more accurate optical measurements.

In regard to claims 25-27, Simonsen discloses all the claimed limitations except the special substantially linear geometry comprises substantially unequal spacing which comprises substantially logarithmic spacing/ progressive spacing. However, Simonsen discloses various detector arrangements (Figs. 7-12 and 15) comprising an unequal spacing configuration (Fig. 11). It is known that the Beer-Lambert law contains exponential relationships of light absorption/ attenuation and the spacing between detectors associated to the light emitter is proportional to the light propagating length. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the spacing between detectors with logarithmic spacing/ progressive spacing through experiments or mathematical relationships to yield predictable results.

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12. Claims 16-18 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen as applied to claims 8 and 29 above, and further in view of Toida (USPGPUB 2002/0052547 – cited in previous action). In regard to claims 16-18 and 32, Simonsen as modified by Wilcken discloses the optical source comprises at least one set of sources comprising at least one light emitting diode and other semi-conductor light sources (Col 5 lines 6-37 of Simonsen) and the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm (Col 5 lines 6-37 of Simonsen). However, Simonsen as modified by Wilcken does not specifically disclose at least one super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm. Toida teaches a super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm ([0007] and [0025]). Simonsen discloses the light emitting diode or other semi-conductor light sources emitting discrete wavelengths can be used in order to reduce the cost of the apparatus. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute one of the light emitting diode or one of other semi-conductor light sources emitting light in approximately 1650 to approximately 1800 nm (Simonsen as modified by Wilcken) with the SLD (Toida) to yield predictable results.

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***Response to Arguments***

13. Applicant's amendment and argument with respect to claims 1-21 and 23-35 filed on 06/05/2014 have been fully considered but they are deemed to be moot in views of the new grounds of rejection.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHU CHUAN (JJ) LIU whose telephone number is (571)270-5507. The examiner can normally be reached on M-TH 8:00am~4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tse Chen can be reached on (571)272-3672. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.




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/CHU CHUAN (JJ) LIU/  
Examiner, Art Unit 3777

/TSE CHEN/  
Supervisory Patent Examiner, Art Unit 3777

<b><i>Index of Claims</i></b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777


✓	<b>Rejected</b>	-	<b>Cancelled</b>	N	<b>Non-Elected</b>	A	<b>Appeal</b>
=	<b>Allowed</b>	÷	<b>Restricted</b>	I	<b>Interference</b>	O	<b>Objected</b>

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant		<input type="checkbox"/> CPA		<input type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47			
CLAIM		DATE							
Final	Original	09/17/2012	04/02/2013	09/19/2013	02/21/2014	06/12/2014			
	1	✓	✓	✓	✓	✓			
	2	✓	✓	✓	✓	✓			
	3	✓	✓	✓	✓	✓			
	4	✓	✓	✓	✓	✓			
	5	✓	✓	✓	✓	✓			
	6	✓	✓	✓	✓	✓			
	7	✓	✓	✓	✓	✓			
	8	✓	✓	✓	✓	✓			
	9	✓	✓	✓	✓	✓			
	10	✓	✓	✓	✓	✓			
	11	✓	✓	✓	✓	✓			
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	34	✓	✓	✓	✓	✓			
	35		✓	✓	✓	✓			
	36			✓	✓	-			

<b><i>Index of Claims</i></b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

✓	<b>Rejected</b>	-	<b>Cancelled</b>	N	<b>Non-Elected</b>	A	<b>Appeal</b>
=	<b>Allowed</b>	÷	<b>Restricted</b>	I	<b>Interference</b>	O	<b>Objected</b>

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant		<input type="checkbox"/> CPA		<input type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47			
CLAIM		DATE							
Final	Original	09/17/2012	04/02/2013	09/19/2013	02/21/2014	06/12/2014			
	37			✓	-	-			
	38			✓	-	-			
	39			✓	✓	-			
	40			✓	-	-			
	41			✓	-	-			
	42			✓	✓	-			
	43			✓	-	-			
	44			✓	-	-			

<b>Search Notes</b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
600	310, 316, 322, 323, 326, 340, 344, 473, 476	09/17/2012	CCL
356	41	09/17/2012	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	04/02/2013	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	09/19/2013	CCL
250	208.1,214	09/19/2013	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	02/21/2014	CCL
330	308	02/21/2014	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	06/12/2014	CCL

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor Name Search (PALM, EAST)	09/10/2012	CCL
East Search (TEXT, USPGPUB, USPAT) See Search History	09/17/2012	CCL
Google NPL Search	09/17/2012	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	04/02/2013	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	09/19/2013	CCL
Google NPL Search	09/19/2013	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	02/21/2014	CCL
Google NPL Search	02/21/2014	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	06/12/2014	CCL
Google NPL Search	06/12/2014	CCL

/CHU CHUAN (JJ) LIU/ Examiner.Art Unit 3777	
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CX-1621

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

/CHU CHUAN (JJ) LIU/  
Examiner.Art Unit 3777

**EAST Search History****EAST Search History (Prior Art)**

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S68	14	photodiode with array with (manufact\$5) and transimpedance	US-PGPUB; USPAT	OR	ON	2014/06/11 13:19
S67	0	photodiode with array with different with (manufact\$5) and transimpedance	US-PGPUB; USPAT	OR	ON	2014/06/11 13:19
S66	1	photodiode with array with different with (characteristic response dynamic) and transimpedance	US-PGPUB; USPAT	OR	ON	2014/06/11 13:08
S65	1	("5767538").PN.	US-PGPUB; USPAT	OR	OFF	2014/06/11 13:04
S64	71	photodiode with array with different with (characteristic response dynamic)	US-PGPUB; USPAT	OR	ON	2014/06/11 12:57

**EAST Search History (Interference)**

< This search history is empty >

**6/ 12/ 2014 9:59:40 AM**

**C:\ Users\ cliu\ Documents\ EAST\ Workspaces\ 12534827.wsp**

Doc code: RCEX

Doc description: Request for Continued Examination (RCE)

CX-1621  
PTO/SB/30EFS (07-09)

Approved for use through 07/31/2012. OMB 0851-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

**REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL  
(Submitted Only via EFS-Web)**

Application Number	12534827	Filing Date	2009-08-03	Docket Number (if applicable)	CERCA.002A	Art Unit	3777
First Named Inventor	Jeroen Poeze			Examiner Name	Liu, Chu Chuan		

**This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.**

Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

**SUBMISSION REQUIRED UNDER 37 CFR 1.114**

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on \_\_\_\_\_☐ Other \_\_\_\_\_☒ Enclosed☒ Amendment/Reply☐ Information Disclosure Statement (IDS)☐ Affidavit(s)/ Declaration(s)☐ Other \_\_\_\_\_**MISCELLANEOUS**☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months \_\_\_\_\_  
(Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)☐ Other \_\_\_\_\_**FEES****The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.**☒ The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to  
Deposit Account No 111410**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED**☒ Patent Practitioner Signature☐ Applicant Signature

Doc code: RCEX

CX-1621  
PTO/SB/30EFS (07-09)

Doc description: Request for Continued Examination (RCE)

Approved for use through 07/31/2012. OMB 0651-0031  
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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Signature of Registered U.S. Patent Practitioner			
Signature	/Scott Cromar/	Date (YYYY-MM-DD)	2014-06-05
Name	Scott Cromar	Registration Number	65066

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*



## Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal				
<b>Application Number:</b>	12534827			
<b>Filing Date:</b>	03-Aug-2009			
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze			
<b>Filer:</b>	Scott Cromar/Daniella Kellogg			
<b>Attorney Docket Number:</b>	CERCA.002A			
Filed as Large Entity				
<b>Utility under 35 USC 111(a) Filing Fees</b>				
<b>Description</b>	<b>Fee Code</b>	<b>Quantity</b>	<b>Amount</b>	<b>Sub-Total in USD(\$)</b>
<b>Basic Filing:</b>				
<b>Pages:</b>				
<b>Claims:</b>				
<b>Miscellaneous-Filing:</b>				
<b>Petition:</b>				
<b>Patent-Appeals-and-Interference:</b>				
<b>Post-Allowance-and-Post-Issuance:</b>				
<b>Extension-of-Time:</b>				

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Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
<b>Miscellaneous:</b>				
RCE - 2nd and Subsequent Request	1820	1	1700	1700
<b>Total in USD (\$)</b>				<b>1700</b>

CX-1621

<b>Electronic Acknowledgement Receipt</b>	
<b>EFS ID:</b>	19223703
<b>Application Number:</b>	12534827
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	1308
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	20995
<b>Filer:</b>	Scott Cromar/Sandra Autry
<b>Filer Authorized By:</b>	Scott Cromar
<b>Attorney Docket Number:</b>	CERCA.002A
<b>Receipt Date:</b>	05-JUN-2014
<b>Filing Date:</b>	03-AUG-2009
<b>Time Stamp:</b>	20:28:12
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$1700
RAM confirmation Number	9026
Deposit Account	111410
Authorized User	KNOBBE MARTENS OLSON AND BEAR
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)</p>	

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**Appx57703**

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**File Listing:**

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		resp_CERCA-002A.pdf	73644 01808a79d2ca5a416f1e35872365cfcca06597e3	yes	11
	Multipart Description/PDF files in .zip description				
	Document Description		Start		End
	Amendment Submitted/Entered with Filing of CPA/RCE		1		1
	Claims		2		6
	Applicant Arguments/Remarks Made in an Amendment		7		11
Warnings:					
Information:					
2	Request for Continued Examination (RCE)	RCE_CERCA-002A.pdf	697843 aa05eaa592896f17bb5f5a68f77392c32bf057cc	no	3
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30318 768e8456f7ca59f222a53b1a45d2d63f47b84344	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			801805		
<p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b> If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b> If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b> If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>					

CERCA.002A

PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Inventor	:	Jeroen Poeze et al.
App. No.	:	12/534,827
Filed	:	August 3, 2009
For	:	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
Examiner	:	Liu, Chu Chuan
Art Unit	:	3777
Conf. No.	:	1308

**RESPONSE TO FINAL OFFICE ACTION DATED MARCH 6, 2014**  
**AND REQUEST FOR CONTINUED EXAMINATION**

**Mail Stop RCE**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In response to the Final Office Action dated March 6, 2014, Applicants respectfully submit the following comments in connection with the above-captioned application.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 2 of this paper.

**Remarks** begin on page 7 of this paper.

**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

### AMENDMENTS TO THE CLAIMS

1. **(Currently Amended)** A noninvasive device configured to produce a signal responsive to light attenuated by tissue at a measurement site, the device comprising:

an optical source configured to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm at tissue of a measurement site; and

a plurality of photodetectors arranged in a spatial configuration that provides a variation in path lengths between at least some of the photodetectors and the optical source, each of said plurality of photodetectors comprising:

two or more photodiodes each having characteristics different from one another and each configured to detect the optical radiation from said optical source after attenuation by said tissue of said measurement site and to output a respective signal stream responsive to said detected optical radiation; and

a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes, wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio and accounting for the characteristics of the two or more photodiodes,

wherein each of said plurality of photodetectors is configured to output a combined and amplified signal stream.

2. **(Original)** The device of claim 1, wherein the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm.

3. **(Original)** The device of claim 1, wherein the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm.

4. **(Original)** The device of claim 3, wherein the optical source is configured to emit optical radiation at three wavelengths about 30 nm apart.

5. **(Original)** The device of claim 3, wherein the optical source is configured to emit optical radiation at about 1610 nm, about 1645 nm, and about 1665 nm.

**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

6. **(Previously Presented)** The device of claim 1, further comprising a patient monitor configured to process the plurality of combined and amplified output signal streams to determine output values for one or more physiological parameters.

7. **(Original)** The device of claim 6, wherein one of the one or more physiological parameters comprises glucose.

8. **(Currently Amended)** A noninvasive, physiological sensor configured to output a signal responsive to a blood analyte present in a monitored patient, said sensor comprising:

a sensor housing;

an optical source coupled to said housing, said optical source configured to transmit a sequence of optical radiation at a tissue site of a patient when said housing is applied to the patient; and

a plurality of photodetectors coupled to said housing, said plurality of photodetectors arranged in a spatial geometry that provides a variation in path lengths between at least some of the photodetectors and the optical source, each of said plurality of photodetectors comprising:

two or more photodiodes each having characteristics different from one another and each configured to detect the sequence of optical radiation from said optical source after attenuation by tissue of said tissue site, each of said two or more photodiodes configured to produce a respective signal stream responsive to said detected sequence of optical radiation; and

a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams produced by the two or more photodiodes, wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio and accounting for the characteristics of the two or more photodiodes,

wherein each of said plurality of photodetectors is configured to output a detection signal responsive to one or more of the signal streams produced by each photodetector's respective single transimpedance amplifier, and wherein said detection signals are usable to determine a blood analyte based at least in part on the variation in path lengths.



**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

9. **(Previously Presented)** The sensor of claim 8, wherein the blood analyte comprises glucose, wherein the sensor further comprises electronic circuitry configured to receive said detection signals responsive to said one or more of the signal streams, and wherein said detection signals are indicative of said glucose.

10. **(Original)** The sensor of claim 8, comprising a display coupled to the sensor housing and configured to display information indicating the blood analyte.

11. **(Previously Presented)** The sensor of claim 8, further comprising a signal medium that is configured to connect to a processing device.

12. **(Previously Presented)** The sensor of claim 8, further comprising an interface configured to provide the detection signals to a device external to the sensor.

13. **(Previously Presented)** The sensor of claim 12, wherein the interface comprises at least one transimpedance amplifier configured to amplify the detection signals from the photodetectors.

14. **(Previously Presented)** The sensor of claim 12, wherein the interface comprises at least one switched capacitor circuit configured to convert said detection signals from the photodetectors into digital information.

15. **(Previously Presented)** The sensor of claim 8, wherein the housing comprises a shell constructed of material adapted to reflect at least some of the optical radiation back into the tissue site.

16. **(Previously Presented)** The sensor of claim 8, wherein the optical source comprises at least one set of sources comprising at least one light emitting diode and at least one super-luminescent light emitting diode.

17. **(Original)** The sensor of claim 16, wherein the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm.

18. **(Original)** The sensor of claim 16, wherein the super-luminescent light emitting diode is configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm.

19. **(Original)** The sensor of claim 8, wherein the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site.

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**Filing Date:** August 3, 2009

20. **(Previously Presented)** The sensor of claim 8, further comprising an optical noise reducer configured to reduce ambient light from entering the tissue site.

21. **(Original)** The sensor of claim 8, further comprising a heat sink configured to dissipate heat from the sensor.

22. **(Canceled)**

23. **(Previously Presented)** The sensor of claim 8, wherein the spatial geometry comprises a substantially linear geometry.

24. **(Previously Presented)** The sensor of claim 23, wherein the substantially linear geometry comprises substantially equal spacing.

25. **(Previously Presented)** The sensor of claim 23, wherein the substantially linear geometry comprises substantially unequal spacing.

26. **(Previously Presented)** The sensor of claim 23, wherein the substantially linear geometry comprises substantially logarithmic spacing.

27. **(Previously Presented)** The sensor of claim 23, wherein the substantially linear geometry comprises substantially progressive spacing.

28. **(Previously Presented)** The sensor of claim 8, wherein the spatial geometry comprises a substantially grid geometry.

29. **(Currently Amended)** A method of measuring an analyte based on multiple streams of optical radiation measured from a measurement site, said method comprising:

emitting, from an optical source, a sequence of optical radiation pulses to the a measurement site;

detecting with a first photodetector at a first location a first stream of optical radiation from the measurement site;

detecting with a second photodetector at a second location different from the first location a second stream of optical radiation from the measurement site; and

determining an output measurement value indicative of an analyte based on the detected streams of optical radiation,

wherein each of said first and second photodetectors comprises:

**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

two or more photodiodes each having characteristics different from one another and each configured to output a signal in response to detected optical radiation; and

a transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signals output by the two or more photodiodes, wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio and accounting for the characteristics of the two or more photodiodes,

wherein said first and second photodetectors are arranged in a spatial configuration that provides a difference in path lengths between the first and second photodetectors and the optical source.

30. **(Original)** The method of claim 29, wherein said analyte comprises glucose.

31. **(Original)** The method of claim 29, further comprising converting the detected streams of optical radiation into a digital signal including a respective stream for each location.

32. **(Original)** The method of claim 29, wherein said emitting comprises emitting light from at least one light emitting diode and at least one super-luminescent light emitting diode.

33. **(Original)** The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 900 to approximately 1300 nm.

34. **(Original)** The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 1650 to approximately 1800 nm.

35. **(Previously Presented)** The device of claim 1, wherein the spatial configuration of the photodetectors comprises at least one of: a substantially linear configuration, a substantially linear configuration including substantially equal spacing, a substantially linear configuration including substantially unequal spacing, a substantially linear configuration including substantially logarithmic spacing, a substantially linear configuration including substantially progressive spacing, and a substantially grid geometry.

36-44. **(Canceled)**

**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

### REMARKS

By way of summary, Claims 1-21 and 23-36, 39, and 42 were pending in this application. In the present response, Applicant has amended Claims 1, 8, and 29, and canceled Claims 36, 39, and 42 without prejudice or disclaimer of subject matter. Accordingly, Claims 1-21 and 23-36, 39, and 42 remain pending for consideration.

#### **Rejection of Claims 1-21 and 23-44 Under 35 U.S.C. § 103(a)**

The Office Action rejected Claims 1-2, 6-13, 15, 19-21, 23-24, 28-31, and 33-36, 39, and 42 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,676,143 to Simonsen et al. (“Simonsen”) in view of U.S. Patent Appl. Pub. No. 2006/0076473 to Wilcken et al. (“Wilcken”); Claims 3-5 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen and Wilcken, and further in view of U.S. Patent No. 5,222,496 to Clarke et al. (“Clarke”); Claims 14 and 25-27 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen and Wilcken, and further in view of U.S. Patent No. 4,114,604 to Shaw et al. (“Shaw”); and Claims 16-18 and 32 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen in view of U.S. Patent Application Publication No. 2002/0052547 to Toida (“Toida”). Applicant respectfully traverses these rejections, the characterization of the pending claims, and each and every implicit and/or explicit reliance on Official Notice. However, in order to advance prosecution Applicant has amended Claims 1, 8, and 29. Applicants respectfully assert that the pending claims are patentable over the cited references for at least the following reasons.

Independent Claims 1, 8, and 29, while varying in scope, each recite “two or more photodiodes each having characteristics different from one another,” and “wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio and accounting for the characteristics of the two or more photodiodes.” Neither Simonsen nor Wilcken, nor a combination of the two, teaches or suggests “two or more photodiodes each having characteristics different from one another” coupled to a single transimpedance amplifier that is “impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio and accounting for the characteristics of the two or more photodiodes.” Rather, while Wilcken discloses a “photodetector array ... positioned to produce electrical signals ... [that] are collected and summed [by] a summing pre-amplifier ...

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and couple[d] to a [transimpedance amplifier] assembly,” (Wilcken, para. [0025])) Wilcken does not disclose multiple photodiodes each having characteristics different from one another. Further, even assuming the photodetector array of Wilcken includes multiple photodiodes having characteristics different from one another (which the Applicant does not concede), Wilcken still fails to disclose the transimpedance amplifier assembly being impedance matched to the “photodetector array” in order to achieve a desired signal-to-noise ratio and to account for differing characteristics among the photodiodes. Accordingly, Simonsen and Wilcken fail to teach or suggest at least the above-mentioned limitations of the claims.

As explained in the Applicant’s previous response, certain advantages of such impedance matching to achieve a desired signal-to-noise ratio and account from differences among characteristics of the photodiodes were not recognized in the prior art. Examples of such advantages are described in, for example, paragraphs [0270]-[0286] of the present application. For example, the present application discloses:

Due to the low-noise requirements for measuring blood analytes like glucose and the challenge of using multiple photodiodes in detector 106, the applicants developed a noise model to assist in configuring front-end 108. Conventionally, those skilled in the art have focused on optimizing the impedance of the transimpedance amplifiers to minimize noise.

However, the following noise model was discovered by the applicants:

$$\text{Noise} = \sqrt{aR + bR^2}, \text{ where:}$$

aR is characteristic of the impedance of the transimpedance amplifier; and

bR<sup>2</sup> is characteristic of the impedance of the photodiodes in detector and the number of photodiodes in detector 106.

*The foregoing noise model was found to be helpful at least in part due to the high SNR required to measure analytes like glucose. However, the foregoing noise model was not previously recognized by artisans at least in part because, in conventional devices, the major contributor to noise was generally believed to originate from the emitter or the LEDs. Therefore, artisans have generally continued to focus on reducing noise at the emitter.*

*However, for analytes like glucose, the discovered noise model revealed that one of the major contributors to noise was generated by the photodiodes. In addition, the amount of noise varied based on the number of photodiodes coupled to a transimpedance amplifier. Accordingly, combinations of various photodiodes from different manufacturers, different impedance values with the transimpedance amplifiers, and different numbers of photodiodes were tested as possible embodiments. (¶¶ [0270]-[0275]; emphasis added.)*

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Additionally,

As noted, FIG. 15J illustrates an exemplary noise model that may be useful in configuring transimpedance amplifiers. As shown, for a given number of photodiodes and a desired SNR, an optimal impedance value for a transimpedance amplifier could be determined.

For example, an exemplary “4 PD per stream” sensor 1502 is shown where detector 106 comprises four photodiodes 1502. The photodiodes 1502 are coupled to a single transimpedance amplifier 1504 to produce an output stream 1506. In this example, the transimpedance amplifier comprises 10 M $\Omega$  resistors 1508 and 1510. Thus, output stream 1506 is produced from the four photodiodes (PD) 1502. As shown in the graph of FIG. 15J, the model indicates that resistance values of about 10 M $\Omega$  may provide an acceptable SNR for analytes like glucose. (¶¶ [0279]-[0280].)

As neither Simonsen nor Wilcken, nor any of the other cited references, teaches or suggests “two or more photodiodes each having characteristics different from one another,” and “a single transimpedance amplifier coupled to the two or more photodiodes, ... wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio and accounting for the characteristics of the two or more photodiodes” (among other limitations), Applicant respectfully asserts that the present claims are patentable over the cited references.

Accordingly, Applicant requests withdrawal of the § 103(a) rejections of independent Claims 1, 8, and 29. Applicant additionally requests withdrawal of the rejections of the remaining dependent claims for at least similar reasons, and for the additional patentable features recited by each.

#### **Request For Telephone Interview**

In view of the forgoing, the present application is believed to be in condition for allowance, and such allowance is respectfully requested. If further issues remain to be resolved, the Applicant’s undersigned attorney of record hereby formally requests a telephone interview with the Examiner. The Applicant’s attorney can be reached at (949) 721-2812 or at the number listed below.

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**No Disclaimers or Disavowals**

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

**Co-Pending Applications of Assignee**

Applicant wishes to draw the Examiner's attention to the following co-pending applications of the present application's assignee.

<b>Docket No.</b>	<b>Serial No.</b>	<b>Title</b>	<b>Filed</b>
CERCA.002C1	12/829325	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	07/01/2010
CERCA.003D1	14/153895	MULTI-STREAM SENSOR FRONT ENDS FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	01/13/2014
CERCA.004C1	13/525166	MULTI-STREAM SENSOR FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	06/15/2012
CERCA.004C3	14/064055	MULTI-STREAM SENSOR FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	10/25/2013
CERCA.005A	12/534825	MULTI-STREAM EMITTER FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	08/03/2009
CERCA.006C1	14/069974	NOISE SHIELDING FOR A NONINVASIVE DEVICE	11/01/2013

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CERCA.007C1	13/888266	CONTOURED PROTRUSION FOR IMPROVING SPECTROSCOPIC MEASUREMENT OF BLOOD CONSTITUENTS	05/06/2013
CERCA.008C1	14/227230	EMITTER DRIVER FOR NONINVASIVE PATIENT MONITOR	03/27/2014
CERCA.011A	12/497506	HEAT SINK FOR NONINVASIVE MEDICAL SENSOR	07/02/2009

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: June 5, 2014

By: /Scott Cromar/\_\_\_\_\_  
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18130107



CX-1621

PTO/SB/06 (09-11)

Approved for use through 1/31/2014. OMB 0651-0032  
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

<b>PATENT APPLICATION FEE DETERMINATION RECORD</b> Substitute for Form PTO-875				Application or Docket Number <b>12/534,827</b>		Filing Date <b>08/03/2009</b>		<input type="checkbox"/> To be Mailed		
ENTITY: <input checked="" type="checkbox"/> LARGE <input type="checkbox"/> SMALL <input type="checkbox"/> MICRO										
<b>APPLICATION AS FILED – PART I</b>										
(Column 1)		(Column 2)								
FOR	NUMBER FILED	NUMBER EXTRA			RATE (\$)	FEE (\$)				
<input type="checkbox"/> BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A			N/A					
<input type="checkbox"/> SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A			N/A					
<input type="checkbox"/> EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A			N/A					
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*			X \$ =					
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*			X \$ =					
<input type="checkbox"/> APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).									
<input type="checkbox"/> MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))										
* If the difference in column 1 is less than zero, enter "0" in column 2.					TOTAL					
<b>APPLICATION AS AMENDED – PART II</b>										
(Column 1)		(Column 2)		(Column 3)						
<b>AMENDMENT</b>	<b>06/05/2014</b>	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)			
	Total (37 CFR 1.16(i))	* 34	Minus	** 43	= 0	X \$80 =	0			
	Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X \$420 =	0			
	<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))									
	<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))									
						TOTAL ADD'L FEE <b>0</b>				
(Column 1)		(Column 2)		(Column 3)						
<b>AMENDMENT</b>		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)			
	Total (37 CFR 1.16(i))	*	Minus	**	=	X \$ =				
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X \$ =				
	<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))									
	<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))									
						TOTAL ADD'L FEE				
<p>* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.</p> <p>** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".</p> <p>*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".</p> <p>The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.</p>										

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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CX-1621



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/534,827	08/03/2009	Jeroen Poeze	CERCA.002A	1308

20995	7590	03/06/2014
KNOBBE MARTENS OLSON & BEAR LLP		
2040 MAIN STREET		
FOURTEENTH FLOOR		
IRVINE, CA 92614		

EXAMINER	
LIU, CHU CHUAN	

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
03/06/2014	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jayna.cartee@knobbe.com  
 efiling@knobbe.com

CX-1621

<b>Office Action Summary</b>	<b>Application No.</b> 12/534,827		<b>Applicant(s)</b> POEZE ET AL.	
	<b>Examiner</b> CHU CHUAN (JJ) LIU		<b>Art Unit</b> 3777	<b>AIA (First Inventor to File) Status</b> No

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 01/07/2014.  
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on \_\_\_\_.

2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims\***

5) ☒ Claim(s) 1-21,23-36,39 and 42 is/are pending in the application.  
5a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.

6) ☐ Claim(s) \_\_\_\_ is/are allowed.

7) ☒ Claim(s) 1-21,23-36,39 and 42 is/are rejected.

8) ☐ Claim(s) \_\_\_\_ is/are objected to.

9) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

\* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see [http://www.uspto.gov/patents/init\\_events/pph/index.jsp](http://www.uspto.gov/patents/init_events/pph/index.jsp) or send an inquiry to [PPHfeedback@uspto.gov](mailto:PPHfeedback@uspto.gov).

**Application Papers**

10) ☐ The specification is objected to by the Examiner.

11) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

**Priority under 35 U.S.C. § 119**

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

**Certified copies:**

a) ☐ All    b) ☐ Some\*\*    c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)  
Paper No(s)/Mail Date 01/07/2014.

3) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.

4) ☐ Other: \_\_\_\_.

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### **DETAILED ACTION**

1. The present application is being examined under the pre-AIA first to invent provisions.
2. Applicant's amendments/ remarks filed on 01/07/2014 have been fully considered.
3. Claims 1-21, 23-36, 39, and 42 are pending for examination. Claims 22, 37-38, 40-41, and 43-44 are canceled.

### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-2, 6-13, 15, 19-21, 23-24, 28-31, 33-36, 39, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen et al (USPN 5,676,143 - cited in previous action) in view of Wilcken et al. (USPGPUB 2006/0076473- cited in previous action). In regard to claims 1, 8, and 29, Simonsen discloses a noninvasive, physiological sensor and a method capable of outputting a signal responsive to a blood analyte present in a monitored patient (Figs. 13-15, 17-18, and 20), said sensor comprising: a sensor housing (Figs. 13-15 and 17-18); an optical source coupled to said housing (elements 27, 29 and 35, Fig. 13; elements 27 and 59, Fig. 17), said optical source configured to transmit a sequence of optical radiation a tissue site of a patient

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when said housing is applied to the patient (Figs. 13-15 and 17-18) and to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm at tissue of a measurement site (Col 5 lines 1-62); and a plurality of photo-detecting sites (Figs. 15 and 19), said plurality of photo-detecting sites arranged in a spatial geometry that provides variation in path lengths between at least some of the photodetectors from-and the optical source (Figs. 15 and 19; Figs. 7-12), each of said plurality of photo-detecting sites comprising: two or more optical fibers each configured to detect the sequence of optical radiation from said optical source after attenuation by tissue of said tissue site (Figs. 15 and 19 and associated descriptions), each of said two or more optical fibers configured to produce a respective optical signal stream responsive to said detected sequence of optical radiation (Figs. 15, 19, and 20); and an amplifier coupled to the two or more optical fibers (Col 18 lines 29-55 and Fig. 20), the amplifier configured to amplify the optical signal streams transmitted by the two or more optical fibers, wherein each of said plurality of optical fibers is configured to output a detection signal responsive to one or more of the signal streams produced by each photodetector's respective single amplifier (Fig. 20; Note that the same detection rows of optical fibers are respectively connected to one of the photodiodes 70a-70c in order to obtain optical information from the same optical path lengths), and wherein said detection signals are usable to determine a blood analyte based at least in part on the variation in path lengths (abstract and Col 9 lines 4-23). Simonsen does not specifically disclose the use of a plurality of photodetectors at each photo-detecting sites and each of said plurality of photodetectors comprises two or more photodiodes. It is well known in the art that using

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a photodiode(s) to detect optical signal is equivalent to using an optical fiber(s) to guide the detected light to a photodiode(s) as evidenced by Tsuchiya (Figs. 9A and 9B of USPN 5,441,054). Using photodiodes at each detecting rows/ sites is equivalent to detect optical signals from optical fibers located in each of the detecting rows/ sites (Figs. 15, 19 and 20) which is connected to an amplifier. Furthermore, Simonsen also discloses the use of a detector array to provide electrical signals in each of the detecting rows (Fig. 7 and associated descriptions). It is also known in the art that a row/ column of the array detector can be connected to a transimpedance amplifier in order to obtain detected optical signal(s) as evidenced by Wyles et al. (Fig. 1a of USPN 5,043,820). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the detecting configuration of fibers with a detector array to yield predictable results. Simonsen as modified does not specifically discloses a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes, wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio. Wilcken teaches two alternative configurations (Figs. 4 and 5), wherein one configuration comprises a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes (elements 410 and 514, Fig. 5 and [0030]), wherein the transimpedance amplifier is impedance matched to the two or more photodiodes (impedance matching element comprised in TIA 512,

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[0030] and Fig. 5). It is well known in that art that impedance matching can reduce noise of the signal as evidenced by Seetharaman et al. (USPGPUB 2004/0119542) and therefore changes the SNR. It would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the array detecting configuration (Simonsen as modified) with the single transimpedance amplifier and signal summing/impedance matching configurations (Wilcken) in order to obtain the optimal data representing the detected optical signal(s).

In regard to claims 2 and 33-34, Simonsen as modified by Wilcken discloses the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm; at least one pulse at a wavelength of approximately 1650 to approximately 1800 nm; at least one pulse at a wavelength of approximately 900 to approximately 1300 nm (Col 5 lines 1-62 of Simonsen).

In regard to claims 6-7, Simonsen as modified by Wilcken discloses a patient monitor capable of processing the plurality of combined and amplified signal streams to determine output values for one or more physiological parameters (glucose, abstract; Fig. 20 of Simonsen).

In regard to claims 9, Simonsen as modified by Wilcken discloses the blood analyte comprises glucose, wherein the sensor comprises electronic circuitry configured to receive said signals responsive to said detected sequence of optical radiation and wherein said output signal is indicative of said glucose (Fig. 20 and associated descriptions of Simonsen).

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In regard to claim 10, Simonsen as modified by Wilcken discloses all the claimed limitations except a display coupled to the sensor housing and configured to display information indicating the blood analyte. Simonsen discloses a microcomputer unit (element 74, Fig. 20 of Simonsen) configured to calculate the concentration of blood analyte (abstract of Simonsen). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the sensor to be coupled to a display in order to output/ show the calculation results to the user.

In regard to claim 11, Simonsen as modified by Wilcken discloses a signal medium that is configured to connect to a processing device (Fig. 20 of Simonsen).

In regard to claim 12, Simonsen as modified by Wilcken discloses an interface configured to provide the signal to a device external to the sensor (Fig. 20 of Simonsen).

In regard to claim 13, Simonsen as modified by Wilcken discloses the interface comprises at least one transimpedance amplifier configured to amplify the signal stream from the photodetectors (Fig. 20 of Simonsen).

In regard to claim 15, Simonsen as modified by Wilcken discloses the housing comprises a shell constructed of material capable of reflecting at least some of the optical radiation back into the tissue site (aluminum 53, Fig. 17 of Simonsen).

In regard to claim 19, Simonsen as modified by Wilcken discloses the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site (Col 18, lines 40-49 of Simonsen).



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In regard to claim 20, Simonsen as modified by Wilcken discloses an optical noise reducer capable of reducing ambient light from entering the tissue site (elements 31a and 31b, Fig. 13 and col 18, lines 56-64 of Simonsen).

In regard to claim 21, Simonsen as modified by Wilcken discloses a heat sink configured to dissipate heat from the sensor (aluminum 53, Fig. 17 and Col 19, lines 30-37 of Simonsen).

In regard to claim 23, Simonsen as modified by Wilcken discloses the special geometry comprises a substantially linear geometry (Figs. 7-12 and 15 of Simonsen).

In regard to claim 24, Simonsen as modified by Wilcken discloses the special substantially linear geometry comprises substantially equal spacing (Fig. 10 of Simonsen).

In regard to claim 28, Simonsen as modified by Wilcken discloses the special geometry comprises a substantially grid geometry (Fig. 12 of Simonsen).

In regard to claims 30-31, claims 30-31 encompass the similar scope of the invention as that of the claims 8-9. Therefore, claims 29-31 are rejected on the same ground as the claims 8-9.

In regard to claim 35, claim 35 encompasses the similar scope of the invention as that of the claims 23- 24. Therefore, claim 35 is rejected on the same ground as the claim 23-24.

In regard to claims 36, 39 and 42, Simonsen as modified by Wilcken discloses at least one of the two or more photodiodes has different characteristics than at least another of the two or more photodiodes (although the photodiode illustrated in Fig. 5

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Wilcken utilize the same indication number 410, it is known that even the same type/model of photodiode would have different characteristics due to manufacture impurity).

In regard to claims 37-38, 40-41 and 43-44, Simonsen as modified by Wilcken discloses the single transimpedance amplifier and the two or more photodiodes are matched in order to achieve a desired signal-to-noise ratio (Fig. 5 and [0030-0033] of Wilcken).

6. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Simonsen and Wilcken as applied to claim 1 above, and further in view of Clarke et al. (USPN 5,222,496 - cited in previous action). In regard to claims 3-5, Simonsen as modified by Wilcken discloses all the claimed limitation except the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm; at three wavelengths about 30 nm apart; and at about 1610 nm, about 1645 nm, and about 1665 nm. Clarke teaches to emit three wavelengths of optical radiation between about 1600 to about 1700 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40); at three wavelengths about 30 nm apart (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; and closely spaced wavelengths will be less than about 30nm wide, abstract and Col 3 lines 9-12); and at about 1610 nm, about 1645 nm, and about 1665 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; 1600nm +/- 15nm, abstract; and about 60nm or 30nm wide, Col 3 lines 9-12) for detecting glucose concentration (Col 3 lines 28-40). The wavelengths taught by Clarke are suitable for measuring glucose concentration. Therefore, it would

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have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the wavelengths (Simonsen as modified by Wilcken) with the wavelengths (Clarke) to yield predictable results.

7. Claim 14 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Simonsen and Wilcken as applied to claim 8 above, and further in view of Shaw et al. (USPN 4,114,604 – cited in previous action). In regard to claim 14, Simonsen discloses all the claimed limitations except the interface comprises at least one switched capacitor circuit configured to convert said signal stream from the photodetectors into digital information. Shaw teaches at least one switched capacitor circuit configured to convert said signal stream from the photodetectors into digital information (element 17, Fig. 1 and Col 4 line 62 – Col 5 line 8). Simonsen discloses amplifiers (elements 71a-c and 72a-c) for converting the detected signals into digital signals. Shaw teaches using the operationally connected capacitor which compensates for amplifier drift and spurious outputs from the detector (Col 5 lines 1-8). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the interface (Simonsen) to incorporate the switched capacitor circuit (Shaw) in order to obtain more accurate optical measurements.

In regard to claims 25-27, Simonsen discloses all the claimed limitations except the special substantially linear geometry comprises substantially unequal spacing which comprises substantially logarithmic spacing/ progressive spacing. However, Simonsen discloses various detector arrangements (Figs. 7-12 and 15) comprising an unequal

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spacing configuration (Fig. 11). It is known that the Beer-Lambert law contains exponential relationships of light absorption/ attenuation and the spacing between detectors associated to the light emitter is proportional to the light propagating length. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the spacing between detectors with logarithmic spacing/ progressive spacing through experiments or mathematical relationships to yield predictable results.

8. Claims 16-18 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen as applied to claims 8 and 29 above, and further in view of Toida (USPGPUB 2002/0052547 – cited in previous action). In regard to claims 16-18 and 32, Simonsen as modified by Wilcken discloses the optical source comprises at least one set of sources comprising at least one light emitting diode and other semi-conductor light sources (Col 5 lines 6-37 of Simonsen) and the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm (Col 5 lines 6-37 of Simonsen). However, Simonsen as modified by Wilcken does not specifically disclose at least one super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm. Toida teaches a super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm ([0007] and [0025]). Simonsen discloses the light emitting diode or other semi-conductor light sources emitting discrete wavelengths can be used in order to reduce the cost of

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the apparatus. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute one of the light emitting diode or one of other semi-conductor light sources emitting light in approximately 1650 to approximately 1800 nm (Simonsen as modified by Wilcken) with the SLD (Toida) to yield predictable results.

### ***Response to Arguments***

9. Applicant's amendment and argument with respect to claims 1, 8, and 29 have been fully considered but they are deemed to be moot in views of the new grounds of rejection.

### ***Conclusion***

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHU CHUAN (JJ) LIU whose telephone number is (571)270-5507. The examiner can normally be reached on M-TH 8:00am~4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tse Chen can be reached on (571)272-3672. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TSE CHEN/  
Supervisory Patent Examiner, Art Unit 3777

/CHU CHUAN (JJ) LIU/  
Examiner, Art Unit 3777

<b>Notice of References Cited</b>	Application/Control No. 12/534,827	Applicant(s)/Patent Under Reexamination POEZE ET AL.	
	Examiner CHU CHUAN (JJ) LIU	Art Unit 3777	Page 1 of 1

**U.S. PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-2004/0119542	06-2004	Seetharaman et al.	330/308
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			


**FOREIGN PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

**NON-PATENT DOCUMENTS**

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	


\*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)  
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

<b><i>Index of Claims</i></b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

✓	<b>Rejected</b>	-	<b>Cancelled</b>	N	<b>Non-Elected</b>	A	<b>Appeal</b>
=	<b>Allowed</b>	÷	<b>Restricted</b>	I	<b>Interference</b>	O	<b>Objected</b>

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant						<input type="checkbox"/> CPA		<input type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47	
CLAIM		DATE									
Final	Original	09/17/2012	04/02/2013	09/19/2013	02/21/2014						
	1	✓	✓	✓	✓						
	2	✓	✓	✓	✓						
	3	✓	✓	✓	✓						
	4	✓	✓	✓	✓						
	5	✓	✓	✓	✓						
	6	✓	✓	✓	✓						
	7	✓	✓	✓	✓						
	8	✓	✓	✓	✓						
	9	✓	✓	✓	✓						
	10	✓	✓	✓	✓						
	11	✓	✓	✓	✓						
	12	✓	✓	✓	✓						
	13	✓	✓	✓	✓						
	14	✓	✓	✓	✓						
	15	✓	✓	✓	✓						
	16	✓	✓	✓	✓						
	17	✓	✓	✓	✓						
	18	✓	✓	✓	✓						
	19	✓	✓	✓	✓						
	20	✓	✓	✓	✓						
	21	✓	✓	✓	✓						
	22	✓	✓	-	-						
	23	✓	✓	✓	✓						
	24	✓	✓	✓	✓						
	25	✓	✓	✓	✓						
	26	✓	✓	✓	✓						
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	28	✓	✓	✓	✓						
	29	✓	✓	✓	✓						
	30	✓	✓	✓	✓						
	31	✓	✓	✓	✓						
	32	✓	✓	✓	✓						
	33	✓	✓	✓	✓						
	34	✓	✓	✓	✓						
	35		✓	✓	✓						
	36			✓	✓						



<b><i>Index of Claims</i></b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

✓	<b>Rejected</b>	-	<b>Cancelled</b>	N	<b>Non-Elected</b>	A	<b>Appeal</b>
=	<b>Allowed</b>	÷	<b>Restricted</b>	I	<b>Interference</b>	O	<b>Objected</b>

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant						<input type="checkbox"/> CPA		<input type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47	
CLAIM		DATE									
Final	Original	09/17/2012	04/02/2013	09/19/2013	02/21/2014						
	37			✓	-						
	38			✓	-						
	39			✓	✓						
	40			✓	-						
	41			✓	-						
	42			✓	✓						
	43			✓	-						
	44			✓	-						

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534,827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 1 OF 1	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	5,427,093	06-1995	Ogawa et al.	
	2	6,278,889	08-2001	Robinson	
	3	6,995,400	02-2006	Mizuyoshi	
	4	7,509,153	03-2009	Blank et al.	
	5	7,734,320	06-2012	Al-Ali	
	6	8,437,825	05-2013	Dalvi et al.	
	7	8,515,509	08-2013	Bruinsma et al.	
	8	8,570,503	10-2013	Hung Vo	
	9	8,577,431	11-2013	Lamego et al.	
	10	2009/0030327	01-2009	Chance, Britton	
	11	2009/0105565	04-2009	Xu	
	12	2010/0049018	02-2010	Duffy et al.	
	13	2011/0105865	05-2011	Yu et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>


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Examiner Signature	/Chu Chuan Liu/	Date Considered	02/21/2014
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

Appx57733

<b>Search Notes</b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
600	310, 316, 322, 323, 326, 340, 344, 473, 476	09/17/2012	CCL
356	41	09/17/2012	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	04/02/2013	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	09/19/2013	CCL
250	208.1,214	09/19/2013	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	02/21/2014	CCL
330	308	02/21/2014	CCL

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor Name Search (PALM, EAST)	09/10/2012	CCL
East Search (TEXT, USPGPUB, USPAT) See Search History	09/17/2012	CCL
Google NPL Search	09/17/2012	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	04/02/2013	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	09/19/2013	CCL
Google NPL Search	09/19/2013	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	02/21/2014	CCL
Google NPL Search	02/21/2014	CCL

INTERFERENCE SEARCH
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/CHU CHUAN (JJ) LIU/ Examiner.Art Unit 3777	
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CX-1621

US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

/CHU CHUAN (JJ) LIU/  
Examiner, Art Unit 3777

**EAST Search History****EAST Search History (Prior Art)**

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S63	7	transimpedance adj amplifier with impedance with match\$3 with noise	US-PGPUB; USPAT	OR	ON	2014/02/21 09:39
S62	0	transimpedance adj amplifier with impedance with match\$3 same (signal with noise with ratio SNR)	US-PGPUB; USPAT	OR	ON	2014/02/21 09:12
S61	33	transimpedance adj amplifier with impedance with match\$3 same (photodiode detector photodetector)	US-PGPUB; USPAT	OR	ON	2014/02/21 09:11
S60	69	transimpedance adj amplifier with impedance with match\$3	US-PGPUB; USPAT	OR	ON	2014/02/21 09:07
S59	0	transimpedance adj amplifier with impedance with match\$3 with (SNR singal with noise with ratio)	US-PGPUB; USPAT	OR	ON	2014/02/21 09:07

**EAST Search History (Interference)**

&lt; This search history is empty &gt;

**2/ 21/ 2014 11:13:45 AM****C:\Users\cliu\Documents\EAST\Workspaces\12534827.wsp**

CERCA.002A

PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Inventor	: Jeroen Poeze, et al.
App. No.	: 12/534,827
Filed	: August 3, 2009
For	: MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
Examiner	: Liu, Chu Chuan
Art Unit	: 3777
Conf No.	: 1308

**RESPONSE TO OFFICE ACTION DATED OCTOBER 8, 2013**

**Mail Stop Amendment**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In response to the Office Action dated October 8, 2013, Applicants respectfully submit the following comments in connection with the above-captioned application.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 2 of this paper.

**Remarks** begin on page 8 of this paper.

**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

### AMENDMENTS TO THE CLAIMS

1. **(Currently Amended)** A noninvasive device configured to produce a signal responsive to light attenuated by tissue at a measurement site, the device comprising:

an optical source configured to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm at tissue of a measurement site; and

a plurality of photodetectors arranged in a spatial configuration that provides a variation in path lengths between at least some of the photodetectors and the optical source, each of said plurality of photodetectors comprising:

two or more photodiodes each configured to detect the optical radiation from said optical source after attenuation by said tissue of said measurement site and to output a respective signal stream responsive to said detected optical radiation; and

a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes, wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio,

wherein each of said plurality of photodetectors is configured to output a combined and amplified signal stream.

2. **(Original)** The device of claim 1, wherein the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm.

3. **(Original)** The device of claim 1, wherein the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm.

4. **(Original)** The device of claim 3, wherein the optical source is configured to emit optical radiation at three wavelengths about 30 nm apart.

5. **(Original)** The device of claim 3, wherein the optical source is configured to emit optical radiation at about 1610 nm, about 1645 nm, and about 1665 nm.

6. **(Previously Presented)** The device of claim 1, further comprising a patient monitor configured to process the plurality of combined and amplified output signal streams to determine output values for one or more physiological parameters.

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**Filing Date:** August 3, 2009

7. **(Original)** The device of claim 6, wherein one of the one or more physiological parameters comprises glucose.

8. **(Currently Amended)** A noninvasive, physiological sensor configured to output a signal responsive to a blood analyte present in a monitored patient, said sensor comprising:

a sensor housing;

an optical source coupled to said housing, said optical source configured to transmit a sequence of optical radiation at a tissue site of a patient when said housing is applied to the patient; and

a plurality of photodetectors coupled to said housing, said plurality of photodetectors arranged in a spatial geometry that provides a variation in path lengths between at least some of the photodetectors and the optical source, each of said plurality of photodetectors comprising:

two or more photodiodes each configured to detect the sequence of optical radiation from said optical source after attenuation by tissue of said tissue site, each of said two or more photodiodes configured to produce a respective signal stream responsive to said detected sequence of optical radiation; and

a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams produced by the two or more photodiodes, wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio,

wherein each of said plurality of photodetectors is configured to output a detection signal responsive to one or more of the signal streams produced by each photodetector's respective single transimpedance amplifier, and wherein said detection signals are usable to determine a blood analyte based at least in part on the variation in path lengths.

9. **(Previously Presented)** The sensor of claim 8, wherein the blood analyte comprises glucose, wherein the sensor further comprises electronic circuitry configured to receive said detection signals responsive to said one or more of the signal streams, and wherein said detection signals are indicative of said glucose.



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**Filing Date:** August 3, 2009

10. **(Original)** The sensor of claim 8, comprising a display coupled to the sensor housing and configured to display information indicating the blood analyte.

11. **(Previously Presented)** The sensor of claim 8, further comprising a signal medium that is configured to connect to a processing device.

12. **(Previously Presented)** The sensor of claim 8, further comprising an interface configured to provide the detection signals to a device external to the sensor.

13. **(Previously Presented)** The sensor of claim 12, wherein the interface comprises at least one transimpedance amplifier configured to amplify the detection signals from the photodetectors.

14. **(Previously Presented)** The sensor of claim 12, wherein the interface comprises at least one switched capacitor circuit configured to convert said detection signals from the photodetectors into digital information.

15. **(Previously Presented)** The sensor of claim 8, wherein the housing comprises a shell constructed of material adapted to reflect at least some of the optical radiation back into the tissue site.

16. **(Previously Presented)** The sensor of claim 8, wherein the optical source comprises at least one set of sources comprising at least one light emitting diode and at least one super-luminescent light emitting diode.

17. **(Original)** The sensor of claim 16, wherein the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm.

18. **(Original)** The sensor of claim 16, wherein the super-luminescent light emitting diode is configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm.

19. **(Original)** The sensor of claim 8, wherein the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site.

20. **(Previously Presented)** The sensor of claim 8, further comprising an optical noise reducer configured to reduce ambient light from entering the tissue site.

21. **(Original)** The sensor of claim 8, further comprising a heat sink configured to dissipate heat from the sensor.

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**Filing Date:** August 3, 2009

22. (Canceled)
23. (Previously Presented) The sensor of claim 8, wherein the spatial geometry comprises a substantially linear geometry.
24. (Previously Presented) The sensor of claim 23, wherein the substantially linear geometry comprises substantially equal spacing.
25. (Previously Presented) The sensor of claim 23, wherein the substantially linear geometry comprises substantially unequal spacing.
26. (Previously Presented) The sensor of claim 23, wherein the substantially linear geometry comprises substantially logarithmic spacing.
27. (Previously Presented) The sensor of claim 23, wherein the substantially linear geometry comprises substantially progressive spacing.
28. (Previously Presented) The sensor of claim 8, wherein the spatial geometry comprises a substantially grid geometry.
29. (Currently Amended) A method of measuring an analyte based on multiple streams of optical radiation measured from a measurement site, said method comprising:
- emitting, from an optical source, a sequence of optical radiation pulses to the a measurement site;
  - detecting with a first photodetector at a first location a first stream of optical radiation from the measurement site;
  - detecting with a second photodetector at a second location different from the first location a second stream of optical radiation from the measurement site; and
  - determining an output measurement value indicative of an analyte based on the detected streams of optical radiation,
- wherein each of said first and second photodetectors comprises:
- two or more photodiodes each configured to output a signal in response to detected optical radiation; and
  - a transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signals output by the two or more photodiodes, wherein the transimpedance amplifier is

**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio,

wherein said first and second photodetectors are arranged in a spatial configuration that provides a difference in path lengths between the first and second photodetectors and the optical source.

30. **(Original)** The method of claim 29, wherein said analyte comprises glucose.

31. **(Original)** The method of claim 29, further comprising converting the detected streams of optical radiation into a digital signal including a respective stream for each location.

32. **(Original)** The method of claim 29, wherein said emitting comprises emitting light from at least one light emitting diode and at least one super-luminescent light emitting diode.

33. **(Original)** The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 900 to approximately 1300 nm.

34. **(Original)** The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 1650 to approximately 1800 nm.

35. **(Previously Presented)** The device of claim 1, wherein the spatial configuration of the photodetectors comprises at least one of: a substantially linear configuration, a substantially linear configuration including substantially equal spacing, a substantially linear configuration including substantially unequal spacing, a substantially linear configuration including substantially logarithmic spacing, a substantially linear configuration including substantially progressive spacing, and a substantially grid geometry.

36. **(Previously Presented)** The device of claim 1, wherein at least one of the two or more photodiodes has different characteristics than at least another of the two or more photodiodes.

37-38. **(Canceled)**

39. **(Previously Presented)** The sensor of claim 8, wherein at least one of the two or more photodiodes has different characteristics than at least another of the two or more photodiodes.

40-41. **(Canceled)**

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**Filing Date:** August 3, 2009

42. **(Previously Presented)** The method of claim 29, wherein at least one of the two or more photodiodes has different characteristics than at least another of the two or more photodiodes.

43-44. **(Canceled)**

**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

### REMARKS

By way of summary, Claims 1-21 and 23-44 were pending in this application. In the present response, Applicants have amended Claims 1, 8, and 29, and canceled Claim 37-38, 40-41, and 43-44 without prejudice or disclaimer. Accordingly, Claims 1-21 and 23-36, 39, and 42 remain pending for consideration.

#### **Rejection of Claims 1-21 and 23-44 Under 35 U.S.C. § 103(a)**

The Office Action rejected Claims 1-2, 6-13, 15, 19-21, 23-24, 28-31, and 33-44 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,676,143 to Simonsen et al. (“Simonsen”) in view of U.S. Patent Appl. Pub. No. 2006/0076473 to Wilcken et al. (“Wilcken”); Claims 3-5 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen and Wilcken, and further in view of U.S. Patent No. 5,222,496 to Clarke et al. (“Clarke”); Claims 14 and 25-27 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen and Wilcken, and further in view of U.S. Patent No. 4,114,604 to Shaw et al. (“Shaw”); and Claims 16-18 and 32 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen in view of U.S. Patent Application Publication No. 2002/0052547 to Toida (“Toida”). Applicants respectfully traverse these rejections and any characterizations of the pending claims. However, in order to advance prosecution Applicants have amended Claims 1, 8, and 29 to incorporate limitations similar to those of respective previously pending dependent Claims 37-38, 40-41, and 43-44. Applicants respectfully assert that the pending claims are patentable over the cited references for at least the following reasons.

Independent Claims 1, 8, and 29, while varying in scope, each recite two or more photodiodes coupled to a single transimpedance amplifier, where the transimpedance amplifier is “impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio.” Neither Simonsen nor Wilcken, nor a combination of the two, teaches or suggests two or more photodiodes coupled to a single transimpedance amplifier that is “impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio.” Rather, while Wilcken discloses a “photodetector array ... positioned to produce electrical signals ... [that] are collected and summed [by] a summing pre-amplifier ... and couple[d] to a [transimpedance amplifier] assembly,” the transimpedance amplifier assembly of Wilcken is not disclosed as

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**Filing Date:** August 3, 2009

being impedance matched to the “photodetector array” in order to achieve a desired signal-to-noise ratio.

In contrast, the present claims recite “a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes, wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio.” Certain advantages of such impedance matching to achieve a desired signal-to-noise ratio were not recognized in the prior art. Examples of such advantages are described in, for example, paragraphs [0270]-[0286] of the present application. For example, the present application discloses:

Due to the low-noise requirements for measuring blood analytes like glucose and the challenge of using multiple photodiodes in detector 106, the applicants developed a noise model to assist in configuring front-end 108. Conventionally, those skilled in the art have focused on optimizing the impedance of the transimpedance amplifiers to minimize noise.

However, the following noise model was discovered by the applicants:

$$\text{Noise} = \sqrt{aR + bR^2}, \text{ where:}$$

$aR$  is characteristic of the impedance of the transimpedance amplifier; and

$bR^2$  is characteristic of the impedance of the photodiodes in detector and the number of photodiodes in detector 106.

The foregoing noise model was found to be helpful at least in part due to the high SNR required to measure analytes like glucose. ***However, the foregoing noise model was not previously recognized by artisans at least in part because, in conventional devices, the major contributor to noise was generally believed to originate from the emitter or the LEDs.*** Therefore, artisans have generally continued to focus on reducing noise at the emitter.

However, for analytes like glucose, the discovered noise model revealed that one of the major contributors to noise was generated by the photodiodes. In addition, the amount of noise varied based on the number of photodiodes coupled to a transimpedance amplifier. Accordingly, combinations of various photodiodes from different manufacturers, different impedance values with the transimpedance amplifiers, and different numbers of photodiodes were tested as possible embodiments. (¶¶ [0270]-[0275]; emphasis added.)

Additionally,

As noted, FIG. 15J illustrates an exemplary noise model that may be useful in configuring transimpedance amplifiers. As shown, for a given number of

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photodiodes and a desired SNR, an optimal impedance value for a transimpedance amplifier could be determined.

For example, an exemplary “4 PD per stream” sensor 1502 is shown where detector 106 comprises four photodiodes 1502. The photodiodes 1502 are coupled to a single transimpedance amplifier 1504 to produce an output stream 1506. In this example, the transimpedance amplifier comprises 10 M $\Omega$  resistors 1508 and 1510. Thus, output stream 1506 is produced from the four photodiodes (PD) 1502. As shown in the graph of FIG. 15J, the model indicates that resistance values of about 10 M $\Omega$  may provide an acceptable SNR for analytes like glucose. (¶¶ [0279]-[0280].)

As neither Simonsen nor Wilcken, nor any of the other cited references teaches or suggests “a single transimpedance amplifier coupled to the two or more photodiodes, ... wherein the transimpedance amplifier is impedance matched to the two or more photodiodes in order to achieve a desired signal-to-noise ratio” (among other limitations), Applicants respectfully assert that the present claims are patentable over the cited references.

Accordingly, Applicants respectfully request withdrawal of the § 103(a) rejection of independent Claims 1, 8, and 29. Applicants additionally request withdrawal of the rejection of the remaining dependent claims for at least similar reasons, and for the additional patentable features recited by each.

#### **Request For Telephone Interview**

In view of the forgoing, the present application is believed to be in condition for allowance, and such allowance is respectfully requested. If further issues remain to be resolved, the Applicants’ undersigned attorney of record hereby formally requests a telephone interview with the Examiner. The Applicants’ attorney can be reached at (949) 721-2923 or at the number listed below.

#### **No Disclaimers or Disavowals**

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other

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**Filing Date:** August 3, 2009

broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

**Co-Pending Applications of Assignee**

Applicant wishes to draw the Examiner's attention to the following co-pending applications of the present application's assignee:

<b>Docket No.</b>	<b>Serial No.</b>	<b>Title</b>	<b>Filed</b>
CERCA.002A	12/534827	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	08/03/2009
CERCA.002C1	12/829325	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	07/01/2010
CERCA.003A	12/534812	MULTI-STREAM SENSOR FRONT ENDS FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	08/03/2009
CERCA.004C1	13/525166	MULTI-STREAM SENSOR FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	06/15/2012
CERCA.004C3	14/064055	MULTI-STREAM SENSOR FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	10/25/2013
CERCA.005A	12/534825	MULTI-STREAM EMITTER FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	08/03/2009
CERCA.006A	12/497528	NOISE SHIELDING FOR A NONINVASIVE DEVICE	07/02/2009
CERCA.006C1	14/069974	NOISE SHIELDING FOR A NONINVASIVE DEVICE	11/01/2013
CERCA.007A	12/497523	CONTOURED PROTRUSION FOR IMPROVING SPECTROSCOPIC MEASUREMENT OF BLOOD CONSTITUENTS	07/02/2009



**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

CERCA.007C1	13/888266	CONTOURED PROTRUSION FOR IMPROVING SPECTROSCOPIC MEASUREMENT OF BLOOD CONSTITUENTS	05/06/2013
CERCA.008A	12/875062	EMITTER DRIVER FOR NONINVASIVE PATIENT MONITOR	09/02/2010
CERCA.011A	12/497506	HEAT SINK FOR NONINVASIVE MEDICAL SENSOR	07/02/2009

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: January 7, 2014

By: /Scott Cromar/\_\_\_\_\_  
Scott A. Cromar  
Registration No. 65,066  
Attorney of Record  
Customer No. 20995  
(949) 760-0404

Docket No.: CERCA.002A

Customer No. 20995

---

**INFORMATION DISCLOSURE STATEMENT**

Inventor	:	Jeroen Poeze, et al.
App. No.	:	12/534,827
Filed	:	August 3, 2009
For	:	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
Examiner	:	Liu, Chu Chuan
Art Unit	:	3777
Conf. No.	:	1308

---

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**References and Listing**

Submitted herewith in the above-identified application is an Information Disclosure Statement listing references for consideration. Copies of any listed foreign and non-patent literature references are being submitted.

**Timing of Disclosure**

This Information Disclosure Statement is being filed after receipt of a First Office Action, but before the mailing date of a Final Action and before the mailing date of a Notice of Allowance. This Statement is accompanied by the fees set forth in 37 C.F.R. 1.17(p). The Commissioner is hereby authorized to charge any additional fees which may be required or to credit any overpayment to Account No. 11-1410.

Respectfully submitted,  
KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: January 7, 2014

By: /Scott Cromar/\_\_\_\_\_  
Scott A. Cromar  
Registration No. 65,066  
Attorney of Record  
Customer No. 20995  
(949) 760-0404

16977904

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534,827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 1 OF 1	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	5,427,093	06-1995	Ogawa et al.	
	2	6,278,889	08-2001	Robinson	
	3	6,995,400	02-2006	Mizuyoshi	
	4	7,509,153	03-2009	Blank et al.	
	5	7,734,320	06-2012	Al-Ali	
	6	8,437,825	05-2013	Dalvi et al.	
	7	8,515,509	08-2013	Bruinsma et al.	
	8	8,570,503	10-2013	Hung Vo	
	9	8,577,431	11-2013	Lamego et al.	
	10	2009/0030327	01-2009	Chance, Britton	
	11	2009/0105565	04-2009	Xu	
	12	2010/0049018	02-2010	Duffy et al.	
	13	2011/0105865	05-2011	Yu et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>

16977681  
010714

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

Appx57750

Electronic Patent Application Fee Transmittal				
<b>Application Number:</b>	12534827			
<b>Filing Date:</b>	03-Aug-2009			
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze			
<b>Filer:</b>	Scott Cromar			
<b>Attorney Docket Number:</b>	CERCA.002A			
Filed as Large Entity				
<b>Utility under 35 USC 111(a) Filing Fees</b>				
<b>Description</b>	<b>Fee Code</b>	<b>Quantity</b>	<b>Amount</b>	<b>Sub-Total in USD(\$)</b>
<b>Basic Filing:</b>				
<b>Pages:</b>				
<b>Claims:</b>				
<b>Miscellaneous-Filing:</b>				
<b>Petition:</b>				
<b>Patent-Appeals-and-Interference:</b>				
<b>Post-Allowance-and-Post-Issuance:</b>				
<b>Extension-of-Time:</b>				

CX-1621

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
<b>Miscellaneous:</b>				
Submission- Information Disclosure Stmt	1806	1	180	180
<b>Total in USD (\$)</b>				<b>180</b>

CX-1621

<b>Electronic Acknowledgement Receipt</b>	
<b>EFS ID:</b>	17842336
<b>Application Number:</b>	12534827
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	1308
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	20995
<b>Filer:</b>	Scott Cromar/Gustavo Lopez
<b>Filer Authorized By:</b>	Scott Cromar
<b>Attorney Docket Number:</b>	CERCA.002A
<b>Receipt Date:</b>	07-JAN-2014
<b>Filing Date:</b>	03-AUG-2009
<b>Time Stamp:</b>	18:47:54
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$180
RAM confirmation Number	5354
Deposit Account	111410
Authorized User	KNOBBE MARTENS OLSON AND BEAR
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)</p>	

Page 89 of 614

**Appx57753**

CX-1621

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		OA_Response_CERCA-002A.pdf	73030 bb654a2b3a606f8de914d5290ca0108a3fb50dff	yes	12
	Multipart Description/PDF files in .zip description				
	Document Description		Start		End
	Amendment/Req. Reconsideration-After Non-Final Reject		1		1
	Claims		2		7
	Applicant Arguments/Remarks Made in an Amendment		8		12
Warnings:					
Information:					
2		IDS.pdf	44873 2579a9a2f4d2e50159c31ac9553ca6eca0eb8c12	yes	2
	Multipart Description/PDF files in .zip description				
	Document Description		Start		End
	Transmittal Letter		1		1
	Information Disclosure Statement (IDS) Form (SB08)		2		2
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	30414 ce81bfbce632bfcff89ad83b0066381aed33c6b2	no	2
Warnings:					
Information:					
Total Files Size (in bytes):			148317		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



CX-1621

PTO/SB/06 (09-11)

Approved for use through 1/31/2014. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

<b>PATENT APPLICATION FEE DETERMINATION RECORD</b> Substitute for Form PTO-875				Application or Docket Number <b>12/534,827</b>		Filing Date <b>08/03/2009</b>		<input type="checkbox"/> To be Mailed			
ENTITY: <input checked="" type="checkbox"/> LARGE <input type="checkbox"/> SMALL <input type="checkbox"/> MICRO											
<b>APPLICATION AS FILED – PART I</b>											
(Column 1)		(Column 2)									
FOR	NUMBER FILED	NUMBER EXTRA			RATE (\$)	FEE (\$)					
<input type="checkbox"/> BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A			N/A						
<input type="checkbox"/> SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A			N/A						
<input type="checkbox"/> EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A			N/A						
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*			X \$ =						
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*			X \$ =						
<input type="checkbox"/> APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).										
<input type="checkbox"/> MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))											
* If the difference in column 1 is less than zero, enter "0" in column 2.					TOTAL						
<b>APPLICATION AS AMENDED – PART II</b>											
(Column 1)		(Column 2)		(Column 3)							
<b>AMENDMENT</b>	<b>01/07/2014</b>	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)			
	Total (37 CFR 1.16(i))	* 37	Minus	** 43	= 0	X \$80 =		0			
	Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X \$420 =		0			
	<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))										
	<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))										
					TOTAL ADD'L FEE		<b>0</b>				
(Column 1)		(Column 2)		(Column 3)							
<b>AMENDMENT</b>		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)			
	Total (37 CFR 1.16(i))	*	Minus	**	=	X \$ =					
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X \$ =					
	<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))										
	<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))										
					TOTAL ADD'L FEE						
<p>* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.</p> <p>** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".</p> <p>*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".</p> <p>The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.</p>										LIE /CORALIA BETANCOURT/	

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



## UNITED STATES PATENT AND TRADEMARK OFFICE

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 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/534,827	08/03/2009	Jeroen Poeze	CERCA.002A	1308

20995	7590	10/08/2013
KNOBBE MARTENS OLSON & BEAR LLP		
2040 MAIN STREET		
FOURTEENTH FLOOR		
IRVINE, CA 92614		

EXAMINER	
LIU, CHU CHUAN	

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
10/08/2013	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jayna.cartee@knobbe.com  
 efiling@knobbe.com

CX-1621

<b>Office Action Summary</b>	<b>Application No.</b> 12/534,827	<b>Applicant(s)</b> POEZE ET AL.	
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777	<b>AIA (First Inventor to File) Status</b> No

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 08/08/2013.  
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on \_\_\_\_.

2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

5) ☒ Claim(s) 1-21 and 23-44 is/are pending in the application.  
5a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.

6) ☐ Claim(s) \_\_\_\_ is/are allowed.

7) ☒ Claim(s) 1-21 and 23-44 is/are rejected.

8) ☐ Claim(s) \_\_\_\_ is/are objected to.

9) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

\* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see [http://www.uspto.gov/patents/init\\_events/pph/index.jsp](http://www.uspto.gov/patents/init_events/pph/index.jsp) or send an inquiry to [PPHfeedback@uspto.gov](mailto:PPHfeedback@uspto.gov).

**Application Papers**

10) ☐ The specification is objected to by the Examiner.

11) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

**Priority under 35 U.S.C. § 119**

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

**Certified copies:**

a) ☐ All    b) ☐ Some \*    c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 08/08/2013.

3) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.

4) ☐ Other: \_\_\_\_.

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### **DETAILED ACTION**

1. The present application is being examined under the pre-AIA first to invent provisions.
2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/08/2013 has been entered.
3. Claims 1-21 and 23-44 are pending for examination.

### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-2, 6-13, 15, 19-21, 23-24, 28-31, and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen et al (USPN 5,676,143 - cited in previous action) in view of Wilcken et al. (USPGPUB 2006/0076473). In regard to claims 1, 8, and 29, Simonsen discloses a noninvasive, physiological sensor and a method capable of outputting a signal responsive to a blood analyte present in a monitored patient (Figs. 13-15, 17-18, and 20), said sensor comprising: a sensor

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housing (Figs. 13-15 and 17-18); an optical source coupled to said housing (elements 27, 29 and 35, Fig. 13; elements 27 and 59, Fig. 17), said optical source configured to transmit a sequence of optical radiation a tissue site of a patient when said housing is applied to the patient (Figs. 13-15 and 17-18) and to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm at tissue of a measurement site (Col 5 lines 1-62); and a plurality of photo-detecting sites (Figs. 15 and 19), said plurality of photo-detecting sites arranged in a spatial geometry that provides variation in path lengths between at least some of the photodetectors from-and the optical source (Figs. 15 and 19; Figs. 7-12), each of said plurality of photo-detecting sites comprising: two or more optical fibers each configured to detect the sequence of optical radiation from said optical source after attenuation by tissue of said tissue site (Figs. 15 and 19 and associated descriptions), each of said two or more optical fibers configured to produce a respective optical signal stream responsive to said detected sequence of optical radiation (Figs. 15, 19, and 20); and an amplifier coupled to the two or more optical fibers (Col 18 lines 29-55 and Fig. 20), the amplifier configured to amplify the optical signal streams transmitted by the two or more optical fibers, wherein each of said plurality of optical fibers is configured to output a detection signal responsive to one or more of the signal streams produced by each photodetector's respective single amplifier (Fig. 20; Note that the same detection rows of optical fibers are respectively connected to one of the photodiodes 70a-70c in order to obtain optical information from the same optical path lengths), and wherein said detection signals are usable to determine a blood analyte based at least in part on the variation in path lengths

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(abstract and Col 9 lines 4-23). Simonsen does not specifically disclose the use of a plurality of photodetectors at each photo-detecting sites and each of said plurality of photodetectors comprises two or more photodiodes. It is well known in the art that using a photodiode(s) to detect optical signal is equivalent to using an optical fiber(s) to guide the detected light to a photodiode(s) as evidenced by Tsuchiya (Figs. 9A and 9B of USPN 5,441,054). Using photodiodes at each detecting rows/ sites is equivalent to detect optical signals from optical fibers located in each of the detecting rows/ sites (Figs. 15, 19 and 20) which is connected to an amplifier. Furthermore, Simonsen also discloses the use of a detector array to provide electrical signals in each of the detecting rows (Fig. 7 and associated descriptions). It is also known in the art that a row/ column of the array detector can be connected to a transimpedance amplifier in order to obtain detected optical signal(s) as evidenced by Wyles et al. (Fig. 1a of USPN 5,043,820). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the detecting configuration of fibers with a detector array to yield predictable results. Simonsen as modified does not specifically discloses a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes. Wilcken teaches two alternative configurations (Figs. 4 and 5), wherein one configuration comprises a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes (elements 410 and 514, Fig. 5 and [0030]). Therefore, it would have

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been obvious to one with ordinary skill in the art at the time of the invention was made to modify the array detecting configuration (Simonsen as modified) with the single transimpedance amplifier and signal summing configurations (Wilcken) in order to obtain the data representing the detected optical signal(s).

In regard to claims 2 and 33-34, Simonsen as modified by Wilcken discloses the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm; at least one pulse at a wavelength of approximately 1650 to approximately 1800 nm; at least one pulse at a wavelength of approximately 900 to approximately 1300 nm (Col 5 lines 1-62 of Simonsen).

In regard to claims 6-7, Simonsen as modified by Wilcken discloses a patient monitor capable of processing the plurality of combined and amplified signal streams to determine output values for one or more physiological parameters (glucose, abstract; Fig. 20 of Simonsen).

In regard to claims 9, Simonsen as modified by Wilcken discloses the blood analyte comprises glucose, wherein the sensor comprises electronic circuitry configured to receive said signals responsive to said detected sequence of optical radiation and wherein said output signal is indicative of said glucose (Fig. 20 and associated descriptions of Simonsen).

In regard to claim 10, Simonsen as modified by Wilcken discloses all the claimed limitations except a display coupled to the sensor housing and configured to display information indicating the blood analyte. Simonsen discloses a microcomputer unit (element 74, Fig. 20 of Simonsen) configured to calculate the concentration of blood

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analyte (abstract of Simonsen). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the sensor to be coupled to a display in order to output/ show the calculation results to the user.

In regard to claim 11, Simonsen as modified by Wilcken discloses a signal medium that is configured to connect to a processing device (Fig. 20 of Simonsen).

In regard to claim 12, Simonsen as modified by Wilcken discloses an interface configured to provide the signal to a device external to the sensor (Fig. 20 of Simonsen).

In regard to claim 13, Simonsen as modified by Wilcken discloses the interface comprises at least one transimpedance amplifier configured to amplify the signal stream from the photodetectors (Fig. 20 of Simonsen).

In regard to claim 15, Simonsen as modified by Wilcken discloses the housing comprises a shell constructed of material capable of reflecting at least some of the optical radiation back into the tissue site (aluminum 53, Fig. 17 of Simonsen).

In regard to claim 19, Simonsen as modified by Wilcken discloses the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site (Col 18, lines 40-49 of Simonsen).

In regard to claim 20, Simonsen as modified by Wilcken discloses an optical noise reducer capable of reducing ambient light from entering the tissue site (elements 31a and 31b, Fig. 13 and col 18, lines 56-64 of Simonsen).



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In regard to claim 21, Simonsen as modified by Wilcken discloses a heat sink configured to dissipate heat from the sensor (aluminum 53, Fig. 17 and Col 19, lines 30-37 of Simonsen).

In regard to claim 23, Simonsen as modified by Wilcken discloses the special geometry comprises a substantially linear geometry (Figs. 7-12 and 15 of Simonsen).

In regard to claim 24, Simonsen as modified by Wilcken discloses the special substantially linear geometry comprises substantially equal spacing (Fig. 10 of Simonsen).

In regard to claim 28, Simonsen as modified by Wilcken discloses the special geometry comprises a substantially grid geometry (Fig. 12 of Simonsen).

In regard to claims 30-31, claims 30-31 encompass the similar scope of the invention as that of the claims 8-9. Therefore, claims 29-31 are rejected on the same ground as the claims 8-9.

In regard to claim 35, claim 35 encompasses the similar scope of the invention as that of the claims 23- 24. Therefore, claim 35 is rejected on the same ground as the claim 23-24.

In regard to claims 36, 39 and 42, Simonsen as modified by Wilcken discloses at least one of the two or more photodiodes has different characteristics than at least another of the two or more photodiodes (although the photodiode illustrated in Fig. 5 Wilcken utilize the same indication number 410, it is known that even the same type/ model of photodiode would have different characteristics due to manufacture impurity).

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In regard to claims 37-38, 40-41 and 43-44, Simonsen as modified by Wilcken discloses the single transimpedance amplifier and the two or more photodiodes are matched in order to achieve a desired signal-to-noise ratio (Fig. 5 and [0030-0033] of Wilcken).

3. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Simonsen and Wilcken as applied to claim 1 above, and further in view of Clarke et al. (USPN 5,222,496 - cited in previous action). In regard to claims 3-5, Simonsen as modified by Wilcken discloses all the claimed limitation except the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm; at three wavelengths about 30 nm apart; and at about 1610 nm, about 1645 nm, and about 1665 nm. Clarke teaches to emit three wavelengths of optical radiation between about 1600 to about 1700 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40); at three wavelengths about 30 nm apart (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; and closely spaced wavelengths will be less than about 30nm wide, abstract and Col 3 lines 9-12); and at about 1610 nm, about 1645 nm, and about 1665 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; 1600nm +/- 15nm, abstract; and about 60nm or 30nm wide, Col 3 lines 9-12) for detecting glucose concentration (Col 3 lines 28-40). The wavelengths taught by Clarke are suitable for measuring glucose concentration. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was

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made to substitute the wavelengths (Simonsen as modified by Wilcken) with the wavelengths (Clarke) to yield predictable results.

4. Claim 14 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Simonsen and Wilcken as applied to claim 8 above, and further in view of Shaw et al. (USPN 4,114,604 – cited in previous action). In regard to claim 14, Simonsen discloses all the claimed limitations except the interface comprises at least one switched capacitor circuit configured to convert said signal stream from the photodetectors into digital information. Shaw teaches at least one switched capacitor circuit configured to convert said signal stream from the photodetectors into digital information (element 17, Fig. 1 and Col 4 line 62 – Col 5 line 8). Simonsen discloses amplifiers (elements 71a-c and 72a-c) for converting the detected signals into digital signals. Shaw teaches using the operationally connected capacitor which compensates for amplifier drift and spurious outputs from the detector (Col 5 lines 1-8). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the interface (Simonsen) to incorporate the switched capacitor circuit (Shaw) in order to obtain more accurate optical measurements.

In regard to claims 25-27, Simonsen discloses all the claimed limitations except the special substantially linear geometry comprises substantially unequal spacing which comprises substantially logarithmic spacing/ progressive spacing. However, Simonsen discloses various detector arrangements (Figs. 7-12 and 15) comprising an unequal spacing configuration (Fig. 11). It is known that the Beer-Lambert law contains

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exponential relationships of light absorption/ attenuation and the spacing between detectors associated to the light emitter is proportional to the light propagating length. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the spacing between detectors with logarithmic spacing/ progressive spacing through experiments or mathematical relationships to yield predictable results.

8. Claims 16-18 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen as applied to claims 8 and 29 above, and further in view of Toida (USPGPUB 2002/0052547 – cited in previous action). In regard to claims 16-18 and 32, Simonsen as modified by Wilcken discloses the optical source comprises at least one set of sources comprising at least one light emitting diode and other semi-conductor light sources (Col 5 lines 6-37 of Simonsen) and the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm (Col 5 lines 6-37 of Simonsen). However, Simonsen as modified by Wilcken does not specifically disclose at least one super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm. Toida teaches a super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm ([0007] and [0025]). Simonsen discloses the light emitting diode or other semi-conductor light sources emitting discrete wavelengths can be used in order to reduce the cost of the apparatus. Therefore, it would have been obvious to one with ordinary skill in the art

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at the time of the invention was made to substitute one of the light emitting diode or one of other semi-conductor light sources emitting light in approximately 1650 to approximately 1800 nm (Simonsen as modified by Wilcken) with the SLD (Toida) to yield predictable results.

### ***Response to Arguments***

4. Applicant's arguments, see page 9 of Remarks, filed on 08/08/2013, with respect to claims 1, 6, 8, 15, 20, 29, and 35 have been fully considered and are persuasive. The objection of claims 1, 6, 8, 15, 20, 29, and 35 has been withdrawn.

5. Applicant's amendment and argument with respect to claims 1-21 and 23-35 and new claims 36-44 filed on 08/08/2013 have been fully considered but they are deemed to be moot in views of the new grounds of rejection. It is noted that in the Remarks filed on 08/08/2013, applicant alleged several features from the specification. If those features are essential to the invention, they should be included in the claims.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHU CHUAN (JJ) LIU whose telephone number is (571)270-5507. The examiner can normally be reached on M-TH 7:00am~3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tse Chen can be reached on (571)272-3672. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chu Chuan Liu/  
Examiner, Art Unit 3777

/Tse Chen/  
Supervisory Patent Examiner, Art Unit 3777

<b>Notice of References Cited</b>	Application/Control No. 12/534,827	Applicant(s)/Patent Under Reexamination POEZE ET AL.	
	Examiner CHU CHUAN (JJ) LIU	Art Unit 3777	Page 1 of 1

**U.S. PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-2006/0076473	04-2006	Wilcken et al.	250/214.00A
*	B	US-5,043,820	08-1991	Wyles et al.	348/300
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

**FOREIGN PATENT DOCUMENTS**

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

**NON-PATENT DOCUMENTS**

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

\*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)  
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 1 OF 1	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	5,452,717	09-1995	Branigan et al.	
	2	6,636,759	10-2003	Robinson	
	3	2004/0039272	02-2004	Abdul-Hafiz et al.	
	4	2005/0162761	07-2005	Hargis et al.	
	5	2006/0189859	08-2006	Kiani et al.	
	6	D551,350	09-2007	Lorimer et al.	
	7	D553,248	10-2007	Nguyen	
	8	D562,985	02-2008	Brefka et al.	
	9	D567,125	04-2008	Okabe et al.	
	10	D569,001	05-2008	Omaki	
	11	D569,521	05-2008	Omaki	
	12	2009/0105565	04-2009	Xu	
	13	2010/0049018	02-2010	Duffy et al.	
	14	7,734,320	06-2012	Al-Ali	
	15	6,278,889	08-2013	Robinson	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>

NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>	
	16	European Office Action issued in Application no. 10763901.5 on 01/11/2013.(Attorney Docket No. CERCA.008EP)		

15219363

Examiner Signature	/Chu Chuan Liu/	Date Considered	09/19/2013
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

Appx57771



**EAST Search History****EAST Search History (Prior Art)**


Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S58	114	single with transimpedance with amplifier and (detector diode photodiode) with array	US-PGPUB; USPAT	OR	ON	2013/09/18 07:14
S57	1497	transimpedance with amplifier and (detector diode photodiode) with array	US-PGPUB; USPAT	OR	ON	2013/09/18 07:14
S56	16	S55 and (detector diode photodiode) with array	US-PGPUB; USPAT	OR	ON	2013/09/18 07:04
S55	146	transimpedance with amplifier and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2013/09/18 06:58

**EAST Search History (Interference)**

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**9/ 19/ 2013 8:44:39 AM**

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<b>Search Notes</b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

CPC- SEARCHED		
Symbol	Date	Examiner


CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
600	310, 316, 322, 323, 326, 340, 344, 473, 476	09/17/2012	CCL
356	41	09/17/2012	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	04/02/2013	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	09/19/2013	CCL
250	208.1,214	09/19/2013	CCL

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor Name Search (PALM, EAST)	09/10/2012	CCL
East Search (TEXT, USPGPUB, USPAT) See Search History	09/17/2012	CCL
Google NPL Search	09/17/2012	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	04/02/2013	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	09/19/2013	CCL
Google NPL Search	09/19/2013	CCL


INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

/CHU CHUAN (JJ) LIU/ Examiner.Art Unit 3777	
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<b><i>Index of Claims</i></b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

✓	<b>Rejected</b>	-	<b>Cancelled</b>	N	<b>Non-Elected</b>	A	<b>Appeal</b>
=	<b>Allowed</b>	÷	<b>Restricted</b>	I	<b>Interference</b>	O	<b>Objected</b>

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant										<input type="checkbox"/> CPA		<input type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47	
CLAIM		DATE													
Final	Original	09/17/2012	04/02/2013	09/19/2013											
	1	✓	✓	✓											
	2	✓	✓	✓											
	3	✓	✓	✓											
	4	✓	✓	✓											
	5	✓	✓	✓											
	6	✓	✓	✓											
	7	✓	✓	✓											
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	33	✓	✓	✓											
	34	✓	✓	✓											
	35		✓	✓											
	36			✓											

<b><i>Index of Claims</i></b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

✓	<b>Rejected</b>	-	<b>Cancelled</b>	N	<b>Non-Elected</b>	A	<b>Appeal</b>
=	<b>Allowed</b>	÷	<b>Restricted</b>	I	<b>Interference</b>	O	<b>Objected</b>

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant		<input type="checkbox"/> CPA		<input type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47			
CLAIM		DATE							
Final	Original	09/17/2012	04/02/2013	09/19/2013					
	37			✓					
	38			✓					
	39			✓					
	40			✓					
	41			✓					
	42			✓					
	43			✓					
	44			✓					

PTO/SB/08 Equivalent

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SHEET 1 OF 1	Attorney Docket No.	CERCA.002A

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	3	2004/0039272	02-2004	Abdul-Hafiz et al.	
	4	2005/0162761	07-2005	Hargis et al.	
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FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>

NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.		T <sup>1</sup>
	16	European Office Action issued in Application no. 10763901.5 on 01/11/2013.(Attorney Docket No. CERCA.008EP)		

15219363

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

Electronic Patent Application Fee Transmittal				
<b>Application Number:</b>	12534827			
<b>Filing Date:</b>	03-Aug-2009			
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze			
<b>Filer:</b>	Scott Cromar/Daniella Kellogg			
<b>Attorney Docket Number:</b>	CERCA.002A			
Filed as Large Entity				
<b>Utility under 35 USC 111(a) Filing Fees</b>				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
<b>Basic Filing:</b>				
<b>Pages:</b>				
<b>Claims:</b>				
Claims in Excess of 20	1202	9	80	720
<b>Miscellaneous-Filing:</b>				
<b>Petition:</b>				
<b>Patent-Appeals-and-Interference:</b>				
<b>Post-Allowance-and-Post-Issuance:</b>				
<b>Extension-of-Time:</b>				

CX-1621

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension - 1 month with \$0 paid	1251	1	200	200
<b>Miscellaneous:</b>				
Request for Continued Examination	1801	1	1200	1200
<b>Total in USD (\$)</b>				<b>2120</b>

CX-1621

**Electronic Acknowledgement Receipt**

<b>EFS ID:</b>	16540981
<b>Application Number:</b>	12534827
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	1308
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	20995
<b>Filer:</b>	Scott Cromar/Christina Gaul
<b>Filer Authorized By:</b>	Scott Cromar
<b>Attorney Docket Number:</b>	CERCA.002A
<b>Receipt Date:</b>	08-AUG-2013
<b>Filing Date:</b>	03-AUG-2009
<b>Time Stamp:</b>	17:33:34
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$2120
RAM confirmation Number	4779
Deposit Account	111410
Authorized User	KNOBBE MARTENS OLSON AND BEAR

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

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**Appx57779**



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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		OA_Response.pdf	62525	yes	13
			04ad76d333a599b8043f9cc81b72cd57e011b934		
	Multipart Description/PDF files in .zip description				
	Document Description	Start	End		
	Response After Final Action	1	1		
	Claims	2	7		
	Applicant summary of interview with examiner	8	8		
	Applicant Arguments/Remarks Made in an Amendment	9	13		
Warnings:					
Information:					
2	Request for Continued Examination (RCE)	RCE.pdf	697842	no	3
			a567f6880860fb0be7acfb4ba9e2a1cada25d257		
Warnings:					
Information:					
3		IDS.pdf	36594	yes	2
			85a40b1267608af7b97fcc473f3dbc55fd8fd626		
	Multipart Description/PDF files in .zip description				
	Document Description	Start	End		
	Transmittal Letter	1	1		
	Information Disclosure Statement (IDS) Form (SB08)	2	2		
Warnings:					
Information:					
4	Foreign Reference	EP_OA_Jan_2013-008EP.pdf	1688437	no	4
			c7b31040bb183fc504e9964c22f3396c1a7f94b		
Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	33975	no	2
			76aab43fee05a1815890265891e26bc41e941870		
Warnings:					

Page 110 of 214

<b>Information:</b>	
<b>Total Files Size (in bytes):</b>	2519373
<p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b>          If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b>          If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b>          If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>	

CERCA.002A

PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Inventor	: Jeroen Poeze, et al.
App. No.	: 12/534,827
Filed	: August 3, 2009
For	: MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
Examiner	: Liu, Chu Chuan
Art Unit	: 3777
Conf No.	: 1308

**RESPONSE TO OFFICE ACTION DATED APRIL 11, 2013**

**Mail Stop RCE**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In response to the Final Office Action dated April 11, 2013, Applicants respectfully submit the following comments in connection with the above-captioned application.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 2 of this paper.

**Summary of Interview** begins on page 8 of this paper.

**Remarks** begin on page 9 of this paper.

**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

### AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A noninvasive device ~~capable of producing~~ configured to produce a signal responsive to light attenuated by tissue at a measurement site, the device comprising:

an optical source configured to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm at tissue of a measurement site; and

a plurality of photodetectors arranged in a ~~spacial~~ spatial configuration that provides a variation in path lengths between at least some of the photodetectors and the optical source, each of said plurality of photodetectors comprising:

two or more photodiodes each configured to detect the optical radiation from said optical source after attenuation by said tissue of said measurement site and to output a respective signal stream responsive to said detected optical radiation; and

a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes,

wherein each of said plurality of photodetectors is configured to output a combined and amplified signal stream.

2. **(Original)** The device of claim 1, wherein the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm.

3. **(Original)** The device of claim 1, wherein the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm.

4. **(Original)** The device of claim 3, wherein the optical source is configured to emit optical radiation at three wavelengths about 30 nm apart.

5. **(Original)** The device of claim 3, wherein the optical source is configured to emit optical radiation at about 1610 nm, about 1645 nm, and about 1665 nm.

6. **(Currently amended)** The device of claim 1, further comprising a patient monitor ~~capable of processing~~ configured to process the plurality of combined and amplified output signal streams to determine output values for one or more physiological parameters.

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7. **(Original)** The device of claim 6, wherein one of the one or more physiological parameters comprises glucose.

8. **(Currently amended)** A noninvasive, physiological sensor ~~capable of outputting~~ configured to output a signal responsive to a blood analyte present in a monitored patient, said sensor comprising:

a sensor housing;

an optical source coupled to said housing, said optical source configured to transmit a sequence of optical radiation at a tissue site of a patient when said housing is applied to the patient; and

a plurality of photodetectors coupled to said housing, said plurality of photodetectors arranged in a ~~spacial~~spatial geometry that provides a variation in path lengths between at least some of the photodetectors and the optical source, each of said plurality of photodetectors comprising:

two or more photodiodes each configured to detect the sequence of optical radiation from said optical source after attenuation by tissue of said tissue site, each of said two or more photodiodes configured to produce a respective signal stream responsive to said detected sequence of optical radiation; and

a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams produced by the two or more photodiodes,

wherein each of said plurality of photodetectors is configured to output a detection signal responsive to one or more of the signal streams produced by each photodetector's respective single transimpedance amplifier, and wherein said detection signals are usable to determine a blood analyte based at least in part on the variation in path lengths.

9. **(Previously presented)** The sensor of claim 8, wherein the blood analyte comprises glucose, wherein the sensor further comprises electronic circuitry configured to receive said detection signals responsive to said one or more of the signal streams, and wherein said detection signals are indicative of said glucose.

10. **(Original)** The sensor of claim 8, comprising a display coupled to the sensor housing and configured to display information indicating the blood analyte.

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11. **(Previously presented)** The sensor of claim 8, further comprising a signal medium that is configured to connect to a processing device.
12. **(Previously presented)** The sensor of claim 8, further comprising an interface configured to provide the detection signals to a device external to the sensor.
13. **(Previously presented)** The sensor of claim 12, wherein the interface comprises at least one transimpedance amplifier configured to amplify the detection signals from the photodetectors.
14. **(Previously presented)** The sensor of claim 12, wherein the interface comprises at least one switched capacitor circuit configured to convert said detection signals from the photodetectors into digital information.
15. **(Currently amended)** The sensor of claim 8, wherein the housing comprises a shell constructed of material ~~capable of reflecting~~ adapted to reflect at least some of the optical radiation back into the tissue site.
16. **(Previously presented)** The sensor of claim 8, wherein the optical source comprises at least one set of sources comprising at least one light emitting diode and at least one super-luminescent light emitting diode.
17. **(Original)** The sensor of claim 16, wherein the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm.
18. **(Original)** The sensor of claim 16, wherein the super-luminescent light emitting diode is configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm.
19. **(Original)** The sensor of claim 8, wherein the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site.
20. **(Currently amended)** The sensor of claim 8, further comprising an optical noise reducer ~~capable of reducing~~ configured to reduce ambient light from entering the tissue site.
21. **(Original)** The sensor of claim 8, further comprising a heat sink configured to dissipate heat from the sensor.
22. **(Canceled)**

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23. **(Currently amended)** The sensor of claim [[22]]8, wherein the ~~spacial~~spatial geometry comprises a substantially linear geometry.

24. **(Previously presented)** The sensor of claim 23, wherein the substantially linear geometry comprises substantially equal spacing.

25. **(Previously presented)** The sensor of claim 23, wherein the substantially linear geometry comprises substantially unequal spacing.

26. **(Previously presented)** The sensor of claim 23, wherein the substantially linear geometry comprises substantially logarithmic spacing.

27. **(Previously presented)** The sensor of claim 23, wherein the substantially linear geometry comprises substantially progressive spacing.

28. **(Currently amended)** The sensor of claim [[22]]8, wherein the ~~spacial~~spatial geometry comprises a substantially grid geometry.

29. **(Currently amended)** A method of measuring an analyte based on multiple streams of optical radiation measured from a measurement site, said method comprising:

emitting, from an optical source, a sequence of optical radiation pulses to the a measurement site;

detecting with a first photodetector at a first location a first stream of optical radiation from the measurement site;

detecting with a second photodetector at a second location different from the first location a second stream of optical radiation from the measurement site; and

determining an output measurement value indicative of an analyte based on the detected streams of optical radiation,

wherein each of said first and second photodetectors comprises:

two or more photodiodes each configured to output a signal in response to detected optical radiation; and

a transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signals output by the two or more photodiodes,

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wherein said first and second photodetectors are arranged in a ~~spacial~~spatial configuration that provides a difference in path lengths between the first and second photodetectors and the optical source.

30. **(Original)** The method of claim 29, wherein said analyte comprises glucose.

31. **(Original)** The method of claim 29, further comprising converting the detected streams of optical radiation into a digital signal including a respective stream for each location.

32. **(Original)** The method of claim 29, wherein said emitting comprises emitting light from at least one light emitting diode and at least one super-luminescent light emitting diode.

33. **(Original)** The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 900 to approximately 1300 nm.

34. **(Original)** The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 1650 to approximately 1800 nm.

35. **(Currently amended)** The device of claim 1, wherein the ~~spacial~~spatial configuration of the photodetectors comprises at least one of: a substantially linear configuration, a substantially linear configuration including substantially equal spacing, a substantially linear configuration including substantially unequal spacing, a substantially linear configuration including substantially logarithmic spacing, a substantially linear configuration including substantially progressive spacing, and a substantially grid geometry.

36. **(New)** The device of claim 1, wherein at least one of the two or more photodiodes has different characteristics than at least another of the two or more photodiodes.

37. **(New)** The device of claim 1, wherein the single transimpedance amplifier and the two or more photodiodes are matched.

38. **(New)** The device of claim 37, wherein the single transimpedance amplifier and the two or more photodiodes are matched in order to achieve a desired signal-to-noise ratio.

39. **(New)** The sensor of claim 8, wherein at least one of the two or more photodiodes has different characteristics than at least another of the two or more photodiodes.

40. **(New)** The sensor of claim 8, wherein the single transimpedance amplifier and the two or more photodiodes are matched.



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41. (New) The sensor of claim 40, wherein the single transimpedance amplifier and the two or more photodiodes are matched in order to achieve a particular signal-to-noise ratio.

42. (New) The method of claim 29, wherein at least one of the two or more photodiodes has different characteristics than at least another of the two or more photodiodes.

43. (New) The method of claim 29, wherein the transimpedance amplifier and the two or more photodiodes are matched.

44. (New) The method of claim 43, wherein the transimpedance amplifier and the two or more photodiodes are matched in order to achieve a desired signal-to-noise ratio.

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### **SUMMARY OF INTERVIEW**

A telephone interview was conducted on July 9, 2013 and attended by Examiners Liu and Chen, and Applicants' representatives Jarom Kesler and Scott Cromar. The differences between Claim 1 and the cited art were discussed. No agreement was reached.

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### **REMARKS**

The Applicants thank Examiners Liu and Chen for the July 9, 2013 interview. Prior to entry of this amendment, Claims 1-35 were pending in this application. In the present amendment, Applicants have amended Claims 1, 6, 8, 15, 20, 23, 28-29, and 35, added new Claims 36-44, and cancelled Claim 22 without prejudice or disclaimer. Accordingly, Claims 1-21 and 23-44 remain pending for consideration.

#### **Objections to the Claims**

The Office Action objected to Claims 1, 8, 29, and 35 for the use of the term “spacial.” The Office Action further objected to Claims 1, 6, 8, 15, and 20 for use of the phrase “capable of” because it is not considered as a positive claim language.

In response, Applicants have canceled Claim 22 and amended Claims 1, 8, 23, 28, 29, 35 to replace all instances of “spacial” with “spatial” as suggested by the office action. Further, Applicants respectfully traverse the objection to the use of “capable of” because “capable of” does not fail to positively recite a limitation. While Applicants traverse this objection, Applicants have amended the language of Claims 1, 6, 8, 15, and 20 along the lines suggested by the Office Action in order to speed prosecution of the present Application. Accordingly, Applicants respectfully request withdrawal of the objections to the claims.

#### **Rejection of Claims 1-35 Under 35 U.S.C. § 103(a)**

The Office Action rejected Claims 1-2, 6-13, 15, 19-24, 28-31, and 33-35 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,676,143 to Simonsen et al. (“Simonsen”) in view of U.S. Patent No. 5,632,272 to Diab et al. (“Diab”); Claims 3-5 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen and Diab, and further in view of U.S. Patent No. 5,222,496 to Clarke et al. (“Clarke”); Claims 14 and 25-27 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen and Diab, and further in view of U.S. Patent No. 4,114,604 to Shaw et al. (“Shaw”); and Claims 16-18 and 32 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen in view of U.S. Patent Application Publication No. 2002/0052547 to Toida (“Toida”). Applicants respectfully traverse these rejections for at least the following reasons.

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**Filing Date:** August 3, 2009

Independent Claims 1, 8, and 29, while varying in scope, each recite multiple photodiodes coupled to a single transimpedance amplifier. In contrast, Simonsen teaches that each photodiode is connected to a different amplifier. As none of the cited references teach multiple photodiodes coupled to a single transimpedance amplifier, Applicants respectfully submit that, for this reason alone, the present claims are patentable over the cited references.

The Office Action attempts to make up for the deficiency of Simonsen by citing U.S. Patent No. 5,441,054 to Tsuchiya (“Tsuchiya”) for the proposition that “using a photodiode (s) to detect optical signal is equivalent to using an optical fiber(s) to guide the detected light to a photodiode(s)” (Office Action, p. 4). Even if this proposition is true, which the Applicants do not necessarily concede, Simonsen still fails to teach multiple photodiodes coupled to a single transimpedance amplifier. While Simonsen does teach multiple optical fibers directing light to a single photodiode, in Simonsen only the single photodiode is connected to a particular amplifier. This configuration of Simonsen cannot be equivalent to current claims as the same results cannot be achieved.

For example, as described in paragraphs [0270]-[0286] of the present application, employing multiple photodiodes with varying characteristics, and coupling those photodiodes to a single matched transimpedance amplifier, enables a reduction in a signal-to-noise ratio of a detection signal. For example, the present application discloses that,

...for analytes like glucose, the discovered noise model revealed that one of the major contributors to noise was generated by the photodiodes. In addition, the amount of noise varied based on the number of photodiodes coupled to a transimpedance amplifier. Accordingly, combinations of various photodiodes from different manufacturers, different impedance values with the transimpedance amplifiers, and different numbers of photodiodes were tested as possible embodiments. (§ [0275].)

Additionally,

...the photodiodes in detectors 106 may comprise multiple active areas that are grouped together. In some embodiments, each of these active areas may be provided its own respective transimpedance. This form of pairing may allow a transimpedance amplifier to be better matched to the characteristics of its corresponding photodiode or active area of a photodiode.

As noted, FIG. 15J illustrates an exemplary noise model that may be useful in configuring transimpedance amplifiers. As shown, for a given number of photodiodes and a desired SNR, an optimal impedance value for a transimpedance amplifier could be determined.

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For example, an exemplary “4 PD per stream” sensor 1502 is shown where detector 106 comprises four photodiodes 1502. The photodiodes 1502 are coupled to a single transimpedance amplifier 1504 to produce an output stream 1506. In this example, the transimpedance amplifier comprises 10 M $\Omega$  resistors 1508 and 1510. Thus, output stream 1506 is produced from the four photodiodes (PD) 1502. As shown in the graph of FIG. 15J, the model indicates that resistance values of about 10 M $\Omega$  may provide an acceptable SNR for analytes like glucose. (¶¶ [0278]-[0280].)

A reduction of the signal-to-noise ratio as a result of a combination of multiple photodiodes coupled to a single matched transimpedance amplifier is simply not possible without the multiple photodiodes, and is not made possible by the addition of optical fibers. Thus, the configuration of Simonsen, even in view of Tsuchiya, is not equivalent to the recitations of the current claims. Rather, the configuration of Simonsen, in which multiple optical fibers simply transfer light to a single photodiode and a single amplifier, cannot achieve the same noise reduction benefit as the configuration of the present claims. The conversion of a light signal to an electrical signal performed by the photodiode is not affected by the inclusion of optical fibers. Further, a single photodiode does not have the same properties as multiple photodiodes. Too much light directed to a single photodiode can quickly oversaturate the photodiode. In contrast, multiple photodiodes can be combined to improve the signal-to-noise ratio without oversaturating. As another example, multiple photodiodes can have varying characteristics and can be capable of detecting different wavelengths of light that a single diode is not capable of doing. Thus Simonsen, even in view of Tsuchiya or any of the other cited references, fails to teach or suggest the limitations of the present claims.

Accordingly, Applicants respectfully request withdrawal of the § 103(a) rejection of independent Claims 1, 8, and 29. Applicants additionally request withdrawal of the rejection of the remaining dependent claims for at least the same reasons, and for the additional features recited therein.

#### **Request For Telephone Interview**

In view of the forgoing, the present application is believed to be in condition for allowance, and such allowance is respectfully requested. If further issues remain to be resolved, the Applicants’ undersigned attorney of record hereby formally requests a telephone interview

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with the Examiner. The Applicants' attorney can be reached at (949) 721-2923 or at the number listed below.

**No Disclaimers or Disavowals**

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

**Co-Pending Applications of Assignee**

Applicant wishes to draw the Examiner's attention to the following co-pending applications of the present application's assignee.

<b>Docket No.</b>	<b>Serial No.</b>	<b>Title</b>	<b>Filed</b>
CERCA.002C1	12/829325	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	07/01/2010
CERCA.007C1	13/888266	CONTOURED PROTRUSION FOR IMPROVING SPECTROSCOPIC MEASUREMENT OF BLOOD CONSTITUENTS	05/06/2013

**Application No.:** 12/534,827  
**Filing Date:** August 3, 2009

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: August 8, 2013

By: /Scott Cromar/\_\_\_\_\_  
Scott A. Cromar  
Registration No. 65,066  
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Customer No. 20995  
(949) 760-0404

15290744

Doc code: RCEX

Doc description: Request for Continued Examination (RCE)

CX-1621  
PTO/SB/30EFS (07-09)

Approved for use through 07/31/2012. OMB 0851-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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**REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL  
(Submitted Only via EFS-Web)**

Application Number	12534827	Filing Date	2009-08-03	Docket Number (if applicable)	CERCA.002A	Art Unit	3777
First Named Inventor	Jeroen Poeze			Examiner Name	Liu, Chu Chuan		

**This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.**

Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

**SUBMISSION REQUIRED UNDER 37 CFR 1.114**

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on \_\_\_\_\_☐ Other \_\_\_\_\_☒ Enclosed☒ Amendment/Reply☒ Information Disclosure Statement (IDS)☐ Affidavit(s)/ Declaration(s)☐ Other \_\_\_\_\_**MISCELLANEOUS**☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months \_\_\_\_\_  
(Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)☐ Other \_\_\_\_\_**FEES****The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.**☒ The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to  
Deposit Account No 111410**SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED**☒ Patent Practitioner Signature☐ Applicant Signature



Doc code: RCEX

Doc description: Request for Continued Examination (RCE)

CX-1621

PTO/SB/30EFS (07-09)

Approved for use through 07/31/2012. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Signature of Registered U.S. Patent Practitioner			
Signature	/Scott Cromar/	Date (YYYY-MM-DD)	2013-08-08
Name	Scott Cromar	Registration Number	65066

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

*If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.*

## Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Docket No.: CERCA.002A

Customer No. 20995

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**INFORMATION DISCLOSURE STATEMENT**

Inventor	: Jeroen Poeze, et al.
App. No.	: 12/534,827
Filed	: August 3, 2009
For	: MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
Examiner	: Liu, Chu Chuan
Art Unit	: 3777
Conf. No.	: 1308

---

Mail Stop RCE  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**References and Listing**

Submitted herewith in the above-identified application is an Information Disclosure Statement listing references for consideration. Copies of any listed foreign and non-patent literature references are being submitted.

**Timing of Disclosure**

This Information Disclosure Statement is being filed with an RCE or before receipt of a first office action after an RCE and no fee is required.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 11-1410.

Respectfully submitted,  
KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: August 8, 2013

By: /Scott Cromar/  
Scott A. Cromar, Reg. No. 65,066  
Attorney of Record  
Customer No. 20995  
(949) 760-0404

15241852

CX-1621

PTO/SB/06 (09-11)

Approved for use through 1/31/2014. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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PATENT APPLICATION FEE DETERMINATION RECORD				Application or Docket Number		Filing Date		<input type="checkbox"/> To be Mailed	
Substitute for Form PTO-875				12/534,827		08/03/2009			
ENTITY: <input checked="" type="checkbox"/> LARGE <input type="checkbox"/> SMALL <input type="checkbox"/> MICRO									
APPLICATION AS FILED – PART I									
(Column 1)		(Column 2)							
FOR	NUMBER FILED	NUMBER EXTRA		RATE (\$)		FEE (\$)			
<input type="checkbox"/> BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A					
<input type="checkbox"/> SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A					
<input type="checkbox"/> EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A					
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		X \$ =					
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		X \$ =					
<input type="checkbox"/> APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).								
<input type="checkbox"/> MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))									
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL					
APPLICATION AS AMENDED – PART II									
(Column 1)		(Column 2)		(Column 3)					
AMENDMENT	08/08/2013	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(i))	* 43	Minus	** 43	= 0	X \$80 =		0	
	Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X \$420 =		0	
	<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))								
	<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))								
				TOTAL ADD'L FEE		0			
(Column 1)		(Column 2)		(Column 3)					
AMENDMENT		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)		ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(i))	*	Minus	**	=	X \$ =			
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X \$ =			
	<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))								
	<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))								
				TOTAL ADD'L FEE					
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.									
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".									
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".									
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.									

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



## UNITED STATES PATENT AND TRADEMARK OFFICE

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 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/534,827	08/03/2009	Jeroen Poeze	CERCA.002A	1308

20995	7590	07/18/2013
KNOBBE MARTENS OLSON & BEAR LLP		
2040 MAIN STREET		
FOURTEENTH FLOOR		
IRVINE, CA 92614		

EXAMINER	
LIU, CHU CHUAN	

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
07/18/2013	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jayna.cartee@knobbe.com  
 efiling@knobbe.com

<b><i>Applicant-Initiated Interview Summary</i></b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	12/534,827	POEZE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	CHU CHUAN (JJ) LIU	3777	

All participants (applicant, applicant's representative, PTO personnel):

(1) Chu Chuan Liu. (3) Scott Cromar.

(2) Tse Chen. (4) Jarom Kesler.

Date of Interview: 09 July 2013.

Type: ☒ Telephonic ☐ Video Conference  
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.  
If Yes, brief description: \_\_\_\_\_.

Issues Discussed ☐ 101 ☐ 112 ☐ 102 ☒ 103 ☐ Others  
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: 1.

Identification of prior art discussed: Simonsen 5,676,143.

**Substance of Interview**  
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

During the interview, claim 1 and Fig. 15J of present application and Figs. 15 and 20 of Simonsen '143 were discussed. Examiner explained how the claimed limitations were met based on Figs. 15 and 20 of Simonsen '143. Examiner indicated that an updated search is required when the formal response has been filed.

**Applicant recordation instructions:** The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

**Examiner recordation instructions:** Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

	/Tse Chen/ Supervisory Patent Examiner, Art Unit 3777
--	--

## Summary of Record of Interview Requirements

### Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

### Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews

#### Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

#### 37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,  
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

### Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.



## UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/534,827	08/03/2009	Jeroen Poeze	CERCA.002A	1308

20995	7590	04/11/2013
KNOBBE MARTENS OLSON & BEAR LLP		
2040 MAIN STREET		
FOURTEENTH FLOOR		
IRVINE, CA 92614		

EXAMINER	
LIU, CHU CHUAN	

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
04/11/2013	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jayna.cartee@knobbe.com  
 efiling@knobbe.com



CX-1621

<b>Office Action Summary</b>	<b>Application No.</b> 12/534,827		<b>Applicant(s)</b> KIANI ET AL.	
	<b>Examiner</b> CHU CHUAN (JJ) LIU		<b>Art Unit</b> 3777	<b>AIA (First Inventor to File) Status</b> No

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 28 February 2013.  
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on \_\_\_\_.

2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

5) ☒ Claim(s) 1-35 is/are pending in the application.  
5a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.

6) ☐ Claim(s) \_\_\_\_ is/are allowed.

7) ☒ Claim(s) 1-35 is/are rejected.

8) ☐ Claim(s) \_\_\_\_ is/are objected to.

9) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

\* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see [http://www.uspto.gov/patents/init\\_events/pph/index.jsp](http://www.uspto.gov/patents/init_events/pph/index.jsp) or send an inquiry to [PPHfeedback@uspto.gov](mailto:PPHfeedback@uspto.gov).

**Application Papers**

10) ☐ The specification is objected to by the Examiner.

11) ☒ The drawing(s) filed on 28 February 2013 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

**Priority under 35 U.S.C. § 119**

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

**Certified copies:**

a) ☐ All    b) ☐ Some \*    c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Interim copies:**

a) ☐ All    b) ☐ Some    c) ☐ None of the: Interim copies of the priority documents have been received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 02/20/2013.

3) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.

4) ☐ Other: \_\_\_\_.

Application/Control Number: 12/534,827  
Art Unit: 3777

Page 2

### **DETAILED ACTION**

1. Applicant's amendments/ remarks filed on 02/28/2013 have been fully considered.
2. Claims 1-35 are pending for examination.

### ***Claim Objections***

3. Claims 1, 6, 8, 15, 20, 28-31, and 35 objected to because of the following informalities: In regard to claims 1, 8, 29, and 35, the term "spacial" is suggested to be replaced by "spatial". In regard to claims 1, 6, 8, 15, and 20, the phrase "capable of" is not considered as a positive claim language and it is suggested that the term should be set forth "configured/ adapted to". Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-2, 6-13, 15, 19-24, 28-31, and 33-35 rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen et al (USPN 5,676,143 - cited in previous action) in view of Diab et al. (USPN 5,632,272 – applicant cited). In regard to claims 1, 8, and 29, Simonsen discloses a noninvasive, physiological sensor and a method capable of outputting a signal responsive to a blood analyte present in a monitored patient (Figs.

Application/Control Number: 12/534,827

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Art Unit: 3777

13-15, 17-18, and 20), said sensor comprising: a sensor housing (Figs. 13-15 and 17-18); an optical source coupled to said housing (elements 27, 29 and 35, Fig. 13; elements 27 and 59, Fig. 17), said optical source configured to transmit a sequence of optical radiation a tissue site of a patient when said housing is applied to the patient (Figs. 13-15 and 17-18) and to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm at tissue of a measurement site (Col 5 lines 1-62); and a plurality of photo-detecting sites (Figs. 15 and 19), said plurality of photo-detecting sites arranged in a spacial geometry that provides variation in path lengths between at least some of the photodetectors from-and the optical source (Figs. 15 and 19; Figs. 7-12), each of said plurality of photo-detecting sites comprising: two or more optical fibers each configured to detect the sequence of optical radiation from said optical source after attenuation by tissue of said tissue site (Figs. 15 and 19 and associated descriptions), each of said two or more optical fibers configured to produce a respective optical signal stream responsive to said detected sequence of optical radiation (Figs. 15, 19, and 20); and an amplifier coupled to the two or more optical fibers (Col 18 lines 29-55 and Fig. 20), the amplifier configured to amplify the optical signal streams transmitted by the two or more optical fibers, wherein each of said plurality of optical fibers is configured to output a detection signal responsive to one or more of the signal streams produced by each photodetector's respective single amplifier (Fig. 20; Note that the same detection rows of optical fibers are respectively connected to one of the photodiodes 70a-70c in order to obtain optical information from the same optical path lengths), and wherein said detection signals are usable to determine a

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blood analyte based at least in part on the variation in path lengths (abstract and Col 9 lines 4-23). Simonsen does not specifically disclose the use of a plurality of photodetectors at each photo-detecting sites and each of said plurality of photodetectors comprises two or more photodiodes. It is well known in the art that using a photodiode(s) to detect optical signal is equivalent to using an optical fiber(s) to guide the detected light to a photodiode(s) as evidenced by Tsuchiya (Figs. 9A and 9B of USPN 5,441,054). Using photodiodes at each detecting rows/ sites and directing the detected electrical signals to an amplifier is equivalent to detect optical signals from optical fibers located in each of the detecting rows/ sites and then connect the fibers to a photodiode (Figs. 15, 19 and 20) which is connected to an amplifier. Both methods would produce combined and amplified signals representing the signals obtained from the same path lengths at the detecting rows/ sites. Furthermore, Simonsen also discloses the use of CCD detector array to provide electrical signals in each of the detecting rows (Fig. 7 and associated descriptions). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the detecting configuration of fibers, a photodiode, and an amplifier with the configuration of photodiodes and an amplifier to yield predictable results. Simonsen as modified does not specifically discloses one of the amplifiers connecting to the photodiode (one of the amplifiers connected to photodiode 70a, Fig. 20 and Col 18 lines 29-55) is a transimpedance amplifier. Diab teaches a transimpedance amplifier can be utilized to amplify a composite current detected from a photodetector (Col 36, lines 24-34). Therefore, it would have been obvious to one with ordinary skill in the art at the

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time of the invention was made to substitute one of the amplifiers (Simonsen) with the transimpedance amplifier (Diab) to yield predictable results.

In regard to claims 2 and 33-34, Simonsen as modified by Diab discloses the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm; at least one pulse at a wavelength of approximately 1650 to approximately 1800 nm; at least one pulse at a wavelength of approximately 900 to approximately 1300 nm (Col 5 lines 1-62 of Simonsen).

In regard to claims 6-7, Simonsen as modified by Diab discloses a patient monitor capable of processing the plurality of combined and amplified signal streams to determine output values for one or more physiological parameters (glucose, abstract; Fig. 20 of Simonsen).

In regard to claims 9, Simonsen as modified by Diab discloses the blood analyte comprises glucose, wherein the sensor comprises electronic circuitry configured to receive said signals responsive to said detected sequence of optical radiation and wherein said output signal is indicative of said glucose (Fig. 20 and associated descriptions of Simonsen).

In regard to claim 10, Simonsen as modified by Diab discloses all the claimed limitations except a display coupled to the sensor housing and configured to display information indicating the blood analyte. Simonsen discloses a microcomputer unit (element 74, Fig. 20 of Simonsen) configured to calculate the concentration of blood analyte (abstract of Simonsen). Therefore, it would have been obvious to one with

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ordinary skill in the art at the time of the invention was made to modify the sensor to be coupled to a display in order to output/ show the calculation results to the user.

In regard to claim 11, Simonsen as modified by Diab discloses a signal medium that is configured to connect to a processing device (Fig. 20 of Simonsen).

In regard to claim 12, Simonsen as modified by Diab discloses an interface configured to provide the signal to a device external to the sensor (Fig. 20 of Simonsen).

In regard to claim 13, Simonsen as modified by Diab discloses the interface comprises at least one transimpedance amplifier configured to amplify the signal stream from the photodetectors (Fig. 20 of Simonsen).

In regard to claim 15, Simonsen as modified by Diab discloses the housing comprises a shell constructed of material capable of reflecting at least some of the optical radiation back into the tissue site (aluminum 53, Fig. 17 of Simonsen).

In regard to claim 19, Simonsen as modified by Diab discloses the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site (Col 18, lines 40-49 of Simonsen).

In regard to claim 20, Simonsen as modified by Diab discloses an optical noise reducer capable of reducing ambient light from entering the tissue site (elements 31a and 31b, Fig. 13 and col 18, lines 56-64 of Simonsen).

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In regard to claim 21, Simonsen as modified by Diab discloses a heat sink configured to dissipate heat from the sensor (aluminum 53, Fig. 17 and Col 19, lines 30-37 of Simonsen).

In regard to claim 22, Simonsen as modified by Diab discloses the photodetectors are arranged in a special geometry (Figs. 7-12, 15, and 17-19 of Simonsen).

In regard to claim 23, Simonsen as modified by Diab discloses the special geometry comprises a substantially linear geometry (Figs. 7-12 and 15 of Simonsen).

In regard to claim 24, Simonsen as modified by Diab discloses the special substantially linear geometry comprises substantially equal spacing (Fig. 10 of Simonsen).

In regard to claim 28, Simonsen as modified by Diab discloses the special geometry comprises a substantially grid geometry (Fig. 12 of Simonsen).

In regard to claims 30-31, claims 30-31 encompass the similar scope of the invention as that of the claims 8-9. Therefore, claims 29-31 are rejected on the same ground as the claims 8-9.

In regard to claim 35, claim 35 encompasses the similar scope of the invention as that of the claims 23- 24. Therefore, claim 35 is rejected on the same ground as the claim 23-24.

6. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Simonsen and Diab as applied to claim 1 above, and further in view of

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Clarke et al. (USPN 5,222,496 - cited in previous action). In regard to claims 3-5, Simonsen as modified by Diab discloses all the claimed limitation except the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm; at three wavelengths about 30 nm apart; and at about 1610 nm, about 1645 nm, and about 1665 nm. Clarke teaches to emit three wavelengths of optical radiation between about 1600 to about 1700 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40); at three wavelengths about 30 nm apart (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; and closely spaced wavelengths will be less than about 30nm wide, abstract and Col 3 lines 9-12); and at about 1610 nm, about 1645 nm, and about 1665 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; 1600nm +/- 15nm, abstract; and about 60nm or 30nm wide, Col 3 lines 9-12) for detecting glucose concentration (Col 3 lines 28-40). The wavelengths taught by Clarke are suitable for measuring glucose concentration. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the wavelengths (Simonsen as modified by Diab) with the wavelengths (Clarke) to yield predictable results.

7. Claim 14 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Simonsen and Diab as applied to claim 8 above, and further in view of Shaw et al. (USPN 4,114,604 – cited in previous action). In regard to claim 14, Simonsen discloses all the claimed limitations except the interface comprises at least one switched capacitor circuit configured to convert said signal stream from the



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photodetectors into digital information. Shaw teaches at least one switched capacitor circuit configured to convert said signal stream from the photodetectors into digital information (element 17, Fig. 1 and Col 4 line 62 – Col 5 line 8). Simonsen discloses amplifiers (elements 71a-c and 72a-c) for converting the detected signals into digital signals. Shaw teaches using the operationally connected capacitor which compensates for amplifier drift and spurious outputs from the detector (Col 5 lines 1-8). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the interface (Simonsen) to incorporate the switched capacitor circuit (Shaw) in order to obtain more accurate optical measurements.

In regard to claims 25-27, Simonsen discloses all the claimed limitations except the special substantially linear geometry comprises substantially unequal spacing which comprises substantially logarithmic spacing/ progressive spacing. However, Simonsen discloses various detector arrangements (Figs. 7-12 and 15) comprising an unequal spacing configuration (Fig. 11). It is known that the Beer-Lambert law contains exponential relationships of light absorption/ attenuation and the spacing between detectors associated to the light emitter is proportional to the light propagating length. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the spacing between detectors with logarithmic spacing/ progressive spacing through experiments or mathematical relationships to yield predictable results.

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8. Claims 16-18 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen as applied to claims 8 and 29 above, and further in view of Toida (USPGPUB 2002/0052547 – cited in previous action). In regard to claims 16-18 and 32, Simonsen as modified by Diab discloses the optical source comprises at least one set of sources comprising at least one light emitting diode and other semi-conductor light sources (Col 5 lines 6-37 of Simonsen) and the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm (Col 5 lines 6-37 of Simonsen). However, Simonsen as modified by Diab does not specifically disclose at least one super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm. Toida teaches a super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm ([0007] and [0025]). Simonsen discloses the light emitting diode or other semi-conductor light sources emitting discrete wavelengths can be used in order to reduce the cost of the apparatus. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute one of the light emitting diode or one of other semi-conductor light sources emitting light in approximately 1650 to approximately 1800 nm (Simonsen as modified by Diab) with the SLD (Toida) to yield predictable results.

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***Response to Arguments***

9. Applicant's arguments, see page 9 of Remarks, filed on 02/28/2013, with respect to claims 1, 11, and 16 have been fully considered and are persuasive. The objection of claims 1, 11, and 16 has been withdrawn.

10. Applicant's arguments with respect to claims 1-35 filed on 02/28/2013 have been fully considered but they are deemed to be moot in views of the new grounds of rejection.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHU CHUAN (JJ) LIU whose telephone number is (571)270-5507. The examiner can normally be reached on M-TH 7:00am~3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tse Chen can be reached on (571)272-3672. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chu Chuan Liu/  
Examiner, Art Unit 3777

/Eric Winakur/  
Primary Examiner, Art Unit 3777

<b>Notice of References Cited</b>	Application/Control No. 12/534,827	Applicant(s)/Patent Under Reexamination KIANI ET AL.	
	Examiner CHU CHUAN (JJ) LIU	Art Unit 3777	Page 1 of 1

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*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
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	S					
	T					

**NON-PATENT DOCUMENTS**

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
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\*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)  
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 1 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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**Appx57817**

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 2 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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**Appx57818**

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 3 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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**Appx57819**



PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 4 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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**Appx57820**

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 5 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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	128	7,957,780	06-2011	Lamego et al.	
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	136	8,008,088	08-2011	Bellott et al.	
	137	8,019,400	09-2011	Diab et al.	
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	139	8,029,765	10-2011	Bellott et al.	
	140	8,036,728	10-2011	Diab et al.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English Language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

Appx57821

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 6 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	141	8,046,040	10-2011	Ali et al.	
	142	8,046,041	10-2011	Diab et al.	
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	163	8,229,533	07-2012	Diab et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>

NON PATENT LITERATURE DOCUMENTS
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Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

**Appx57822**

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 7 OF 7	Attorney Docket No.	CERCA.002A

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	164	PCT International Search Report, App. No. PCT/US2010/047899, Date of Actual Completion of Search: 01/26/2011, 4 pages.	
	165	International Preliminary Report on Patentability and Written Opinion of the International Searching Authority issued in Application No. PCT US2009/049638, mailed January 5, 2011 in 9 pages.	
	166	<a href="http://www.masimo.com/rainbow/pronto.htm">http://www.masimo.com/rainbow/pronto.htm</a> Noninvasive & Immediate Hemoglobin Testing, printed on August 20, 2009	
	167	<a href="http://www.masimo.com/pulseOximeter/Rad5.htm">http://www.masimo.com/pulseOximeter/Rad5.htm</a> ; Signal Extraction Pulse Oximeter, printed on August 20, 2009	
	168	<a href="http://blogderoliveira.blogspot.com/2008_02_01_archive.html">http://blogderoliveira.blogspot.com/2008_02_01_archive.html</a> ; Ricardo Oliveira, printed on August 20, 2009	
	169	<a href="http://www.masimo.com/rad-57/">http://www.masimo.com/rad-57/</a> ; Noninvasive Measurement of Methemoglobin, Carboxyhemoglobin and Oxyhemoglobin in the blood. Printed on August 20, 2009	
	170	<a href="http://amivital.ugr.es/blog/?tag+spo2">http://amivital.ugr.es/blog/?tag+spo2</a> ; Monitorizacion de la hemoglobina...y mucho mas, printed on August 20, 2009	
	171	<a href="http://www.masimo.com/spco/">http://www.masimo.com/spco/</a> ; Carboxyhemoglobin Noninvasive > Continuous > Immediate, printed on August 20, 2009	
	172	<a href="http://www.masimo.com/PARTNERS/WELCHALLYN.htm">http://www.masimo.com/PARTNERS/WELCHALLYN.htm</a> ; Welch Allyn Expands Patient Monitor Capabilities with Masimo Pulse Oximetry Technology, printed on August 20, 2009	
	173	<a href="http://www.masimo.com/pulseOximeter/PPO.htm">http://www.masimo.com/pulseOximeter/PPO.htm</a> ; Masimo Personal Pulse Oximeter, printed on August 20, 2009	
	174	<a href="http://www.masimo.com/generalFloor/system.htm">http://www.masimo.com/generalFloor/system.htm</a> ; Masimo Patient SafetyNet System at a Glance, printed on August 20, 2009	
	175	<a href="http://www.masimo.com/partners/GRASEBY.htm">http://www.masimo.com/partners/GRASEBY.htm</a> ; Graseby Medical Limited, printed on August 20, 2009	
	176	International Search Report and Written Opinion for PCT/US2009/049638, mailed January 7, 2010.	


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Examiner Signature	/Chu Chuan Liu/	Date Considered	04/02/2013
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

T<sup>1</sup> - Place a check mark in this area when an English Language Translation is attached.

SIDERED EXCEPT WHERE LINED THROUGH. /CCL/

Appx57823

<b><i>Index of Claims</i></b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

✓	<b>Rejected</b>	-	<b>Cancelled</b>	N	<b>Non-Elected</b>	A	<b>Appeal</b>
=	<b>Allowed</b>	÷	<b>Restricted</b>	I	<b>Interference</b>	O	<b>Objected</b>

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant		<input type="checkbox"/> CPA		<input type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47			
CLAIM		DATE							
Final	Original	09/17/2012	04/02/2013						
	1	✓	✓						
	2	✓	✓						
	3	✓	✓						
	4	✓	✓						
	5	✓	✓						
	6	✓	✓						
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	8	✓	✓						
	9	✓	✓						
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	28	✓	✓						
	29	✓	✓						
	30	✓	✓						
	31	✓	✓						
	32	✓	✓						
	33	✓	✓						
	34	✓	✓						
	35		✓						


**EAST Search History****EAST Search History (Prior Art)**

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S54	183	fiber and (detector photodetector) and 600/310-344.ccls. and reflect\$3 and (tissue skin sample) and jp.inco.	US-PGPUB; USPAT	OR	ON	2013/04/02 08:35
S53	1939	fiber and (detector photodetector) and 600/310-344.ccls. and reflect\$3 and (tissue skin sample)	US-PGPUB; USPAT	OR	ON	2013/04/02 08:24
S52	1	("5676143").PN.	US-PGPUB; USPAT	OR	OFF	2013/04/02 08:19
S51	112	fiber and led and 600/310-344.ccls. and jp.inco.	US-PGPUB; USPAT	OR	ON	2013/04/02 08:13
S50	12	S47 and JP.inco.	US-PGPUB; USPAT	OR	ON	2013/04/02 08:13
S49	10	S48 and JP.inco.	US-PGPUB; USPAT	OR	ON	2013/04/02 08:13
S48	856	S47 and (tissue skin)	US-PGPUB; USPAT	OR	ON	2013/04/02 08:11
S47	892	fiber and led and alternative and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2013/04/02 08:11
S46	8	(detectors photodiodes photodetectors) with transimpedance with amplif\$3 and 600/316.ccls.	US-PGPUB; USPAT	OR	ON	2013/03/27 07:45
S45	64	S43 and transimpedance	US-PGPUB; USPAT	OR	ON	2013/03/27 07:23
S44	286	S43 and amplif\$3	US-PGPUB; USPAT	OR	ON	2013/03/27 07:23
S43	587	pathlength\$3 and detector\$1 and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2013/03/27 07:19
S42	14	pathlength\$3 and far with detector\$1 and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2013/03/27 07:16

**EAST Search History (Interference)**

&lt; This search history is empty &gt;

**4/ 2/ 2013 2:43:36 PM****C:\Users\cliu\Documents\EAST\Workspaces\12534827.wsp**

<b>Search Notes</b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
600	310, 316, 322, 323, 326, 340, 344, 473, 476	09/17/2012	CCL
356	41	09/17/2012	CCL
600	310, 316, 322, 323, 326, 340, 344, 473, 476	04/02/2013	CCL

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor Name Search (PALM, EAST)	09/10/2012	CCL
East Search (TEXT, USPGPUB, USPAT) See Search History	09/17/2012	CCL
Google NPL Search	09/17/2012	CCL
Updated East Search (TEXT, USPGPUB, USPAT) See Search History	04/02/2013	CCL

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

/CHU CHUAN (JJ) LIU/  
Examiner.Art Unit 3777

CERCA.002A

PATENT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor : Jeroen Poeze  
 App. No. : 12/534827  
 Filed : August 3, 2009  
 For : MULTI-STREAM DATA  
 COLLECTION SYSTEM FOR  
 NONINVASIVE MEASUREMENT  
 OF BLOOD CONSTITUENTS  
 Examiner : Chu Chuan Liu  
 Art Unit : 3777  
 Conf No. : 1308

**Certificate Of EFS Web  
Transmission**

I hereby certify that this correspondence, and any other attachment noted on the automated Acknowledgement Receipt, is being transmitted from within the Pacific Time zone to the Commissioner for Patents via the EFS Web server on:

February 28, 2013

(Date)

/Jarom Kesler/

Jarom D. Kesler, Reg. No. 57,046

**RESPONSE TO OFFICE ACTION DATED OCTOBER 1, 2012****Mail Stop Amendment**

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Dear Sir:

In response to the Office Action dated October 1, 2012, Applicants respectfully submit the following comments in connection with the above-captioned application.

**Amendments to the Specification** begin on page 2 of this paper.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 3 of this paper.

**Amendments to the Drawings** begin on page 8 of this paper. A "Replacement Sheet" for the sheet of drawings being amended can be found in the Appendix.

**Remarks/Arguments** begin on page 9 of this paper.



**Application No.:** 12/534827  
**Filing Date:** August 3, 2009

### AMENDMENTS TO THE SPECIFICATION

Changes to the specification are shown below in highlighted form, where insertions appear as underlined text (e.g., insertions) while deletions appear as strikethrough text (e.g., ~~deletions~~) or double brackets (e.g., [[deletions]]).

#### In the Specification:

Please amend the numbered paragraphs as follows:

**[0002]** This application is related to the following U.S. Patent Applications:

<u>App. No.</u>	<u>Filing Date</u>	<u>Title</u>	<u>Attorney Docket</u>
12/497,528	7/12/09	Noise Shielding for Noninvasive Device Contoured Protrusion for Improving	MLHUM.006A
12/497,523	7/12/09	Spectroscopic Measurement of Blood Constituents	MLHUM.007A
12/498,506	7/12/09	Heat Sink for Noninvasive Medical Sensor	MLHUM.011A
<u>12/534,812</u> Unknown	<u>8/3/09</u> Herewith	Multi-Stream Sensor Front Ends for Non-Invasive Measurement of Blood Constituents	MLHUM.003A
<u>12/534,823</u> Unknown	<u>8/3/09</u> Herewith	Multi-Stream Sensor for Non-Invasive Measurement of Blood Constituents	MLHUM.004A
<u>12/534,825</u> Unknown	<u>8/3/09</u> Herewith	Multi-Stream Emitter for Non-Invasive Measurement of Blood Constituents	MLHUM.005A

**Application No.:** 12/534827  
**Filing Date:** August 3, 2009

### AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A noninvasive device capable of producing a signal responsive to light attenuated by tissue at a measurement site, the device comprising:

an optical source configured to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm at tissue of a measurement site; and

a plurality of photodetectors arranged in a spacial configuration that provides a variation in path lengths between at least some of the photodetectors and the optical source, each of said plurality of photodetectors comprising:

two or more photodiodes each configured to detect the optical radiation from said optical source after attenuation by said tissue of said measurement site and each to output a respective signal stream responsive to said detected optical radiation; and

a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes,

wherein each of said plurality of photodetectors is configured to output a combined and amplified signal stream.

2. **(Original)** The device of claim 1, wherein the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm.

3. **(Original)** The device of claim 1, wherein the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm.

4. **(Original)** The device of claim 3, wherein the optical source is configured to emit optical radiation at three wavelengths about 30 nm apart.

5. **(Original)** The device of claim 3, wherein the optical source is configured to emit optical radiation at about 1610 nm, about 1645 nm, and about 1665 nm.

6. **(Currently amended)** The device of claim 1, further comprising a patient monitor capable of processing the plurality of combined and amplified output-signal streams to determine output values for one or more physiological parameters.

7. **(Original)** The device of claim 6, wherein one of the one or more physiological parameters comprises glucose.

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**Filing Date:** August 3, 2009

8. **(Currently amended)** A noninvasive, physiological sensor capable of outputting a signal responsive to a blood analyte present in a monitored patient, said sensor comprising:

a sensor housing;

an optical source positioned by coupled to said housing, said optical source configured to transmit a sequence of optical radiation at with respect to a tissue site of a patient when said housing is applied to the patient; and

a plurality of photodetectors positioned by coupled to said housing, said plurality of photodetectors arranged in a spacial geometry that provides with respect to said tissue site when said housing is applied to the patient with a variation in path lengths among between at least some of the photodetectors from and the optical source, each of said plurality of photodetectors comprising:

two or more photodiodes each the photodetectors configured to detect a the sequence of optical radiation from said optical source after attenuation by tissue of said tissue site, each of said photodetectors two or more photodiodes each configured to output produce a respective signal stream responsive to said detected sequence of optical radiation; and

a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams produced by the two or more photodiodes,

wherein each of said plurality of photodetectors is configured to an output a detection signal responsive to one or more of the signal streams produced by each photodetector's respective single transimpedance amplifier, and wherein said detection signals are is usable to determine the a blood analyte based at least in part on the variation in path lengths.

9. **(Currently amended)** The sensor of claim 8, wherein the blood analyte comprises glucose, wherein the sensor further comprises electronic circuitry configured to receive said detection signals responsive to said detected sequence of optical radiation one or more of the signal streams, and wherein said output detection signals are is indicative of said glucose.

10. **(Original)** The sensor of claim 8, comprising a display coupled to the sensor housing and configured to display information indicating the blood analyte.

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**Filing Date:** August 3, 2009

11. **(Currently amended)** The sensor of claim [[6]]8, further comprising a signal medium that is configured to connect to a processing device.

12. **(Currently amended)** The sensor of claim 8, further comprising an interface configured to provide the detection signals to a device external to the sensor.

13. **(Currently amended)** The sensor of claim 12, wherein the interface comprises at least one transimpedance amplifier configured to amplify the detection signals ~~stream~~ from the photodetectors.

14. **(Currently amended)** The sensor of claim 12, wherein the interface comprises at least one switched capacitor circuit configured to convert said detection signals ~~stream~~ from the photodetectors into digital information.

15. **(Original)** The sensor of claim 8, wherein the housing comprises a shell constructed of material capable of reflecting at least some of the optical radiation back into the tissue site.

16. **(Currently amended)** The sensor of claim [[6]]8, wherein the optical source comprises at least one set of sources comprising at least one light emitting diode and at least one super-luminescent light emitting diode.

17. **(Original)** The sensor of claim 16, wherein the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm.

18. **(Original)** The sensor of claim 16, wherein the super-luminescent light emitting diode is configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm.

19. **(Original)** The sensor of claim 8, wherein the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site.

20. **(Original)** The sensor of claim 8, further comprising an optical noise reducer capable of reducing ambient light from entering the tissue site.

21. **(Original)** The sensor of claim 8, further comprising a heat sink configured to dissipate heat from the sensor.

22. **(Original)** The sensor of claim 8, wherein the photodetectors are arranged in a special geometry.

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**Filing Date:** August 3, 2009

23. **(Currently amended)** The sensor of claim 22, wherein the ~~special~~spacial geometry comprises a substantially linear geometry.

24. **(Currently amended)** The sensor of claim 23, wherein the ~~special~~substantially linear geometry comprises substantially equal spacing.

25. **(Currently amended)** The sensor of claim 23, wherein the ~~special~~substantially linear geometry comprises substantially unequal spacing.

26. **(Currently amended)** The sensor of claim 23, wherein the ~~special~~substantially linear geometry comprises substantially logarithmic spacing.

27. **(Currently amended)** The sensor of claim 23, wherein the ~~special~~substantially linear geometry comprises substantially progressive spacing.

28. **(Currently amended)** The sensor of claim 22, wherein the ~~spacial~~special geometry comprises a substantially grid geometry.

29. **(Currently amended)** A method of measuring an analyte based on multiple streams of optical radiation measured from a measurement site, said method comprising:

emitting, from an optical source, a sequence of optical radiation pulses to ~~the~~a measurement site;

detecting with a first photodetector at a first location a first stream of optical radiation from the measurement site;

detecting with a second photodetector ~~at least at one additional~~ a second location different from the first location ~~an additional~~ a second stream of optical radiation from the measurement site; and

determining an output measurement value indicative of the ~~an~~ analyte based on the detected streams of optical radiation,

wherein each of said first and second photodetectors comprises:

two or more photodiodes each configured to output a signal in response to detected optical radiation; and

a transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signals output by the two or more photodiodes,

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**Filing Date:** August 3, 2009

wherein said first and second photodetectors are arranged in a spacial configuration that provides a difference in path lengths between the first and second photodetectors and the optical source.

30. **(Original)** The method of claim 29, wherein said analyte comprises glucose.

31. **(Original)** The method of claim 29, further comprising converting the detected streams of optical radiation into a digital signal including a respective stream for each location.

32. **(Original)** The method of claim 29, wherein said emitting comprises emitting light from at least one light emitting diode and at least one super-luminescent light emitting diode.

33. **(Original)** The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 900 to approximately 1300 nm.

34. **(Original)** The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 1650 to approximately 1800 nm.

35. **(New)** The device of claim 1, wherein the spacial configuration of the photodetectors comprises at least one of: a substantially linear configuration, a substantially linear configuration including substantially equal spacing, a substantially linear configuration including substantially unequal spacing, a substantially linear configuration including substantially logarithmic spacing, a substantially linear configuration including substantially progressive spacing, and a substantially grid geometry.

**Application No.:** 12/534827  
**Filing Date:** August 3, 2009

#### **AMENDMENTS TO THE DRAWINGS**

The attached sheet of drawings includes changes to Fig. 15J on Sheet 53. Specifically, the graph of Fig. 15J as filed in the present application inadvertently included the incorrect legend. By way of the present amendment, Applicants provide a replacement drawing. The replacement drawing draws support from and is identical to Fig. 1B of App. No. 61/086,108, filed Aug., 4, 2008, to which the present application claims priority, and which is incorporated by reference. Accordingly, Applicants submit that no new matter is added by the present amendment.

**Application No.:** 12/534827  
**Filing Date:** August 3, 2009

### **REMARKS**

The Applicant thanks the Examiner for their examination of the present application. By way of summary, Claims 1-34 were pending in this application. In the present response, the Applicant has amended Claims 1, 6, 8, 9, 11-14, 16, and 23-29, and added new Claim 35. Accordingly, Claims 1-35 remain pending for consideration.

#### **Objections to Claims 1, 11, and 16 for Informalities**

The Office Action objected to Claims 1, 11, and 16 because of various typographical errors. Applicants have amended Claims 1, 11, and 16 to correct the typographical errors, and not for purposes of patentability.

#### **Rejection Of Claims 1-9, 11-13, 15, 19-24, and 28-31 Under 35 U.S.C. §§ 102(b)**

The Office Action rejected Claims 1-7 and 29-31 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,222,496 to Clarke et al. ("Clarke"); and Claims 8-9, 11-13, 15, 19-24, and 28-31 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,676,143 to Simonsen et al. ("Simonsen"). Applicants respectfully traverse these rejections and the characterization of the pending claims. In view of the foregoing amendments and for at least the reasons set forth below, Applicants respectfully request reconsideration of the aforementioned claims.



**Application No.:** 12/534827  
**Filing Date:** August 3, 2009

Independent Claim 1

Independent Claim 1 has been amended to recite:

A noninvasive device capable of producing a signal responsive to light attenuated by tissue at a measurement site, the device comprising:

an optical source configured to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm at tissue of a measurement site; and

**a plurality of photodetectors** arranged in a spacial configuration that provides a variation in path lengths between at least some of the photodetectors and the optical source, **each of said plurality of photodetectors comprising:**

**two or more photodiodes each configured to detect the optical radiation from said optical source** after attenuation by said tissue of said measurement site and to output a respective signal stream responsive to said detected optical radiation; and

**a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams output by the two or more photodiodes,**

**wherein each of said plurality of photodetectors is configured to output a combined and amplified signal stream.**

(emphasis added).

Applicants respectfully submit that Clarke fails to teach all the features of amended Claim 1. Specifically, Clarke fails to teach at least multiple photodiodes feeding a single transimpedance amplifier, and multiple detectors each comprising multiple photodiodes. Rather, Clarke teaches a single detector consisting of optical fibers that transmit light waves to a series of diode detectors. Thus, Clarke fails to teach, a plurality of photodetectors, each comprising two or more photodiodes, the two or more photodiodes of each photodetector coupled to a single transimpedance amplifier configured to combine and amplify the signal streams of the photodiodes.

Accordingly, Applicants respectfully request the Examiner withdraw the rejection of Claim 1 under 35 U.S.C. §§ 102(b). Applicants additionally request that the 102(b) rejections of Claims 2-7, which depend either directly or indirectly from Claim 1, be withdrawn for at least the same reasons, and because of the additional features recited therein.

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Independent Claim 8

Independent Claim 8 has been amended to recite:

A noninvasive, physiological sensor capable of outputting a signal responsive to a blood analyte present in a monitored patient, said sensor comprising:

a sensor housing;

an optical source coupled to said housing, said optical source configured to transmit a sequence of optical radiation at a tissue site of a patient when said housing is applied to the patient; and

**a plurality of photodetectors** coupled to said housing, said plurality of photodetectors arranged in a spacial geometry that provides a variation in path lengths between at least some of the photodetectors and the optical source, **each of said plurality of photodetectors comprising:**

**two or more photodiodes each configured to detect the sequence of optical radiation** from said optical source after attenuation by tissue of said tissue site, each of said two or more photodiodes configured to produce a respective signal stream responsive to said detected sequence of optical radiation; and

**a single transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signal streams produced by the two or more photodiodes,**

**wherein each of said plurality of photodetectors is configured to output a detection signal responsive to one or more of the signal streams produced by each photodetector's respective single transimpedance amplifier,** and wherein said detection signals are usable to determine a blood analyte based at least in part on the variation in path lengths.

(emphasis added).

Applicants respectfully submit that Simonsen fails to teach all the features of amended Claim 8. Specifically, Simonsen fails to teach at least multiple photodiodes feeding a single transimpedance amplifier. Rather, Simonsen teaches that each photodiode feeds a separate amplifier. Thus, Simonsen fails to teach a plurality of photodetectors arranged in a spacial configuration in which each photodetector includes two or more photodiodes coupled to a single transimpedance amplifier.

Accordingly, Applicants respectfully request the Examiner withdraw the rejection of Claim 8 under 35 U.S.C. §§ 102(b). Applicants additionally request that the 102(b) rejections of Claims

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9, 11-13, 15, 19-24, and 28, which depend either directly or indirectly from Claim 8, be withdrawn for at least the same reasons, and because of the additional features recited therein.

Independent Claim 29

Independent Claim 29 has been amended to recite:

A method of measuring an analyte based on multiple streams of optical radiation measured from a measurement site, said method comprising:

emitting, from an optical source, a sequence of optical radiation pulses to a measurement site;

detecting with **a first photodetector at a first location** a first stream of optical radiation from the measurement site;

detecting with **a second photodetector at a second location different from the first location** a second stream of optical radiation from the measurement site; and

determining an output measurement value indicative of an analyte based on the detected streams of optical radiation,

wherein **each of said first and second photodetectors comprises:**

**two or more photodiodes each configured to output a signal in response to detected optical radiation; and**

**a transimpedance amplifier coupled to the two or more photodiodes, the transimpedance amplifier configured to combine and amplify the signals output by the two or more photodiodes,**

wherein said first and second photodetectors are arranged in a spacial configuration that provides a difference in path lengths between the first and second photodetectors and the optical source.

(emphasis added).

For reasons similar to those discussed above with reference to Claims 1 and 8, Applicants respectfully submit that both Clarke and Simonsen fail to teach all the features of amended Claim 29. Specifically, both Clarke and Simonsen fail to teach at least the emphasized limitations. Accordingly, Applicants respectfully request the Examiner withdraw the rejection of Claim 29 under 35 U.S.C. §§ 102(b). Applicants additionally request that the 102(b) rejections of Claims 30 and 31, which depend either directly or indirectly from Claim 29, be withdrawn for at least the same reasons, and because of the additional features recited therein.

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**Rejection Of Claims 10, 14, 16-18, 25-27, and 32-34 Under 35 U.S.C. § 103(a)**

The Office Action rejected Claim 10 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen; Claims 14 and 25-27 under 35 U.S.C. § 103(a) as being unpatentable over Simonsen in view of U.S. Patent No. 4,114,604 to Shaw et al. ("Shaw"); and Claims 16-18 and 32-34 as being unpatentable over Simonsen in view of U.S. Patent Application Publication No. 2002/0052547 to Toida ("Toida"). Applicants respectfully traverse these rejections and the characterization of the pending claims.

As each of Claims 10, 14, 16-18, 25-27, and 32-34 depend, either directly or indirectly, from either Claim 8 or Claim 29, Applicants submit that these claims are patentable for at least the same reasons as those discussed above, and for the additional feature recited therein. Accordingly, Applicants respectfully request the rejections of Claims 10, 14, 16-18, 25-27, and 32-34 under 35 U.S.C. §103(a) be withdrawn.

**Request For Telephone Interview**

In view of the forgoing, the present application is believed to be in condition for allowance, and such allowance is respectfully requested. If further issues remain to be resolved, the Applicants' undersigned attorney of record hereby formally requests a telephone interview with the Examiner. The Applicants' attorney can be reached at (949) 721-2923 or at the number listed below.

**No Disclaimers or Disavowals**

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not

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reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

**Co-Pending Applications of Assignee**

Applicant wishes to draw the Examiner's attention to the following co-pending applications of the present application's assignee.

<b>Docket No.</b>	<b>Serial No.</b>	<b>Title</b>	<b>Filed</b>
CERCA.002A	12/534827	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	08/03/2009
CERCA.003A	12/534812	MULTI-STREAM SENSOR FRONT ENDS FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	08/03/2009
CERCA.004C1	13/525166	MULTI-STREAM SENSOR FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	06/15/2012
CERCA.005A	12/534825	MULTI-STREAM EMITTER FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS	08/03/2009
CERCA.006A	12/497528	NOISE SHIELDING FOR A NONINVASIVE DEVICE	07/02/2009
CERCA.007A	12/497523	CONTOURED PROTRUSION FOR IMPROVING SPECTROSCOPIC MEASUREMENT OF BLOOD CONSTITUENTS	07/02/2009
CERCA.008A	12/875062	EMITTER DRIVER FOR NONINVASIVE PATIENT MONITOR	09/02/2010
CERCA.011A	12/497506	HEAT SINK FOR NONINVASIVE MEDICAL SENSOR	07/02/2009

**Application No.:** 12/534827  
**Filing Date:** August 3, 2009

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: February 28, 2013

By: /Jarom Kesler/  
Jarom D. Kesler  
Registration No. 57,046  
Attorney of Record  
Customer No. 20995  
(949) 760-0404

14601489

Electronic Patent Application Fee Transmittal				
<b>Application Number:</b>	12534827			
<b>Filing Date:</b>	03-Aug-2009			
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze			
<b>Filer:</b>	Scott Cromar			
<b>Attorney Docket Number:</b>	CERCA.002A			
Filed as Large Entity				
<b>Utility under 35 USC 111(a) Filing Fees</b>				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
<b>Basic Filing:</b>				
<b>Pages:</b>				
<b>Claims:</b>				
Claims in Excess of 20	1202	1	62	62
<b>Miscellaneous-Filing:</b>				
<b>Petition:</b>				
<b>Patent-Appeals-and-Interference:</b>				
<b>Post-Allowance-and-Post-Issuance:</b>				
<b>Extension-of-Time:</b>				

CX-1621

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension - 2 months with \$0 paid	1252	1	570	570
<b>Miscellaneous:</b>				
<b>Total in USD (\$)</b>				<b>632</b>



CX-1621

**Electronic Acknowledgement Receipt**

<b>EFS ID:</b>	15086994
<b>Application Number:</b>	12534827
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	1308
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	20995
<b>Filer:</b>	Scott Cromar/Gustavo Lopez
<b>Filer Authorized By:</b>	Scott Cromar
<b>Attorney Docket Number:</b>	CERCA.002A
<b>Receipt Date:</b>	28-FEB-2013
<b>Filing Date:</b>	03-AUG-2009
<b>Time Stamp:</b>	20:19:02
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$632
RAM confirmation Number	10314
Deposit Account	111410
Authorized User	KNOBBE MARTENS OLSON AND BEAR
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)</p>	

Page 180 of 614

**Appx57844**

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File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Drawings-only black and white line drawings	CERCA-002A_ReplaceDrwg.pdf	405855	no	1
			4f01bf7f3564e5636b7440dd2ad935134f72d1a8		
Warnings:					
Information:					
2		CERCA-002A_Response.pdf	567573	yes	15
			dc5d979425383f73f870a19c17c298ae47bffebf		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Amendment/Req. Reconsideration-After Non-Final Reject		1	1	
	Specification		2	2	
	Claims		3	7	
	Drawings-only black and white line drawings		8	8	
	Applicant Arguments/Remarks Made in an Amendment		9	15	
Warnings:					
Information:					
3	Fee Worksheet (SB06)	fee-info.pdf	32417	no	2
			711c53694a4ecc3e273a0e7f2a2cc1b2030095be		
Warnings:					
Information:					
Total Files Size (in bytes):			1005845		

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**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

**National Stage of an International Application under 35 U.S.C. 371**

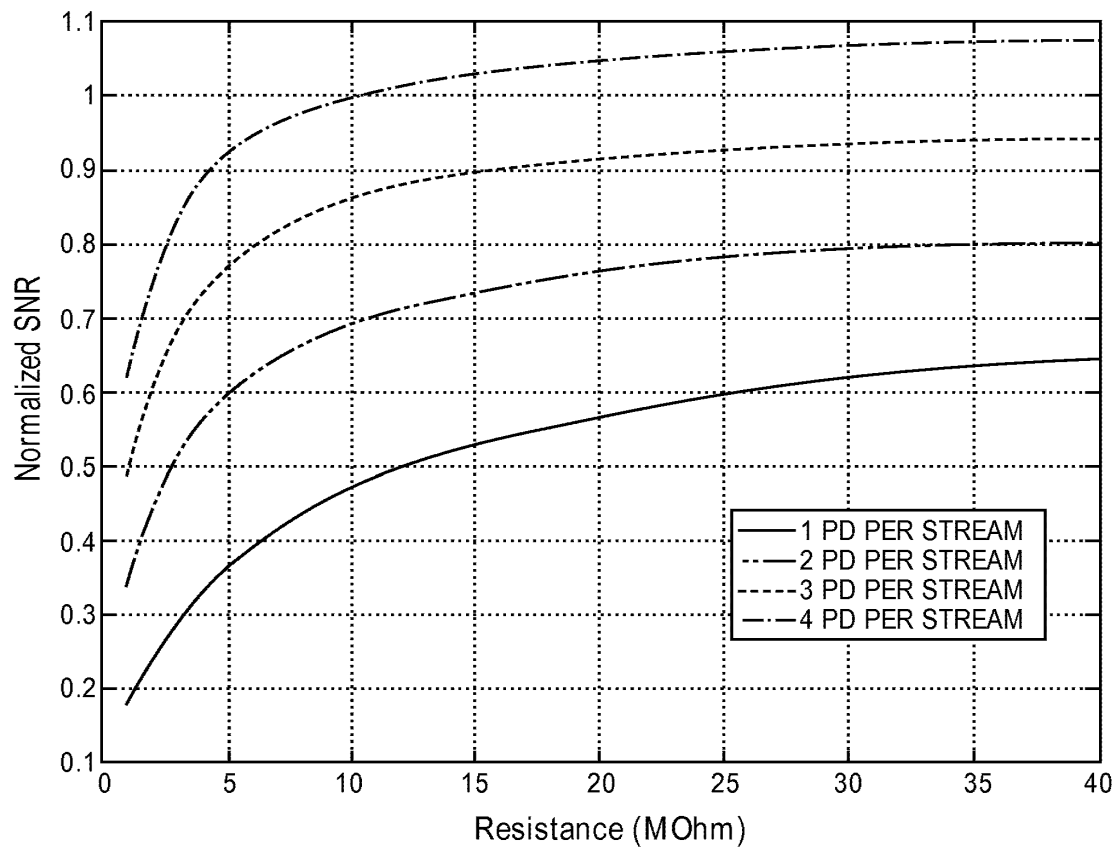
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Replacement Sheet

53/65

**FIG. 15J**

CX-1621

PTO/SB/06 (07-06)

Approved for use through 1/31/2007. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

<b>PATENT APPLICATION FEE DETERMINATION RECORD</b> Substitute for Form PTO-875					Application or Docket Number <b>12/534,827</b>		Filing Date <b>08/03/2009</b>		<input type="checkbox"/> To be Mailed	
<b>APPLICATION AS FILED – PART I</b>										
(Column 1)			(Column 2)			SMALL ENTITY <input type="checkbox"/> OR		OTHER THAN SMALL ENTITY		
FOR	NUMBER FILED	NUMBER EXTRA	RATE (\$)	FEE (\$)	OR	RATE (\$)	FEE (\$)			
<input type="checkbox"/> BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A				
<input type="checkbox"/> SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A				
<input type="checkbox"/> EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A				
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X \$ =		OR	X \$ =				
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X \$ =			X \$ =				
<input type="checkbox"/> APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).									
<input type="checkbox"/> MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))										
* If the difference in column 1 is less than zero, enter "0" in column 2.										
<b>APPLICATION AS AMENDED – PART II</b>										
(Column 1)			(Column 2)			SMALL ENTITY OR		OTHER THAN SMALL ENTITY		
AMENDMENT	02/28/2013	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE (\$)	ADDITIONAL FEE (\$)	OR	RATE (\$)	ADDITIONAL FEE (\$)	
	Total (37 CFR 1.16(i))	* 35	Minus	** 34	= 1	X \$ =		OR	X \$62=	
	Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X \$ =		OR	X \$250=	
<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))										
<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))										
TOTAL ADD'L FEE						OR	TOTAL ADD'L FEE			
							<b>62</b>			
(Column 1)			(Column 2)			SMALL ENTITY OR		OTHER THAN SMALL ENTITY		
AMENDMENT	Total (37 CFR 1.16(i))	* 35	Minus	** 34	= 1	X \$ =		OR	X \$ =	
	Independent (37 CFR 1.16(h))	* 3	Minus	***3	= 0	X \$ =		OR	X \$ =	
<input type="checkbox"/> Application Size Fee (37 CFR 1.16(s))										
<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))										
TOTAL ADD'L FEE						OR	TOTAL ADD'L FEE			
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.										
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".										
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".										
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.										

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 1 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	2002/0016536	02-2002	Benni, Paul	
	2	2002/0039272	04-2002	Abdul-Hafiz et al.	
	3	2002/0091322	07-2002	Chaiken et al.	
	4	2002/0115918	08-2002	Crowley, Robert J.	
	5	2004/0054269	03-2004	Rantala et al.	
	6	2006/0167347	07-2006	Xu et al.	
	7	2006/0211924	09-2006	Dalke et al.	
	8	2006/0208191	09-2006	Kessler et al.	
	9	2006/0258922	11-2006	Mason et al.	
	10	2007/0149865	06-2007	Laakkonen	
	11	2007/0165218	07-2007	Qing et al.	
	12	2007/0197886	08-2007	Naganuma et al.	
	13	2007/0293792	12-2007	Sliwa et al.	
	14	2008/0036855	02-2008	Heenan, Adam John	
	15	2008/0071154	03-2008	Hausmann et al.	
	16	2008/0139908	06-2008	Kurth	
	17	2008/0130232	06-2008	Yamamoto	
	18	2008/0208006	08-2008	Farr	
	19	2009/0043180	02-2009	Tschautscher et al.	
	20	2009/0163775	06-2009	Barrett et al.	
	21	2010/0004518	01-2010	Vo et al.	
	22	2010/0049018	02-2010	Duffy et al.	
	23	2010/0090118	04-2010	Rozenfeld, Anatoly	
	24	D326,715	06-1992	Schmidt, Michael	
	25	D356,870	03-1995	Ivers et al.	
	26	D378,414	03-1997	Allen et al.	
	27	D390,666	02-1998	Lagerlof, Ingemar	
	28	D403,070	12-1998	Maeda et al.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English Language Translation is attached.

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 2 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	29	D414,870	10-1999	Saltzstein et al.	
	30	D452,012	12-2001	Phillips, Barney L.	
	31	D455,834	04-2002	Oonars et al.	
	32	D463,561	09-2002	Fukatsu et al.	
	33	D481,459	10-2003	Nahm, Werner	
	34	D502,655	03-2005	Huang, Chun-Mu	
	35	D508,862	08-2005	Behar et al.	
	36	D510,625	10-2005	Widener et al.	
	37	D514,461	02-2006	Harju, Jonne	
	38	D535,031	01-2007	Barrett et al.	
	39	D537,164	02-2007	Shigemori et al.	
	40	D547,454	07-2007	Hsieh, Chin-Chih	
	41	D549,830	08-2007	Behar et al.	
	42	D550,364	09-2007	Glover et al.	
	43	D551,350	09-2007	Lorimer et al.	
	44	D553,248	10-2007	Nguyen	
	45	D562,985	02-2008	Brefka et al.	
	46	D567,125	04-2008	Okabe et al.	
	47	D569,001	05-2008	Oamki	
	48	D603,966	11-2009	Jones et al.	
	49	D614,305	04-2010	Al-Ali et al.	
	50	D621,516	08-2010	Kiani et al.	
	51	RE41,317	05-2010	Parker	
	52	RE41,912	11-2010	Parker	
	53	RE42,753	09-2011	Kiani-Azarbayjany et al.	
	54	RE43,169	02-2012	Parker	
	55	4,444,471	04-1984	Ford et al.	
	56	4,655,225	04-1987	Dahne et al.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 3 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	57	4,755,676	07-1988	Gaalema et al.	
	58	4,880,304	11-1989	Jaeb et al.	
	59	5,035,243	07-1991	Muz, Edwin	
	60	5,069,214	12-1991	Samaras et al.	
	61	5,131,391	07-1992	Sakai et al.	
	62	5,159,929	11-1992	Morris et al.	
	63	5,222,295	06-1993	Clarke et al.	
	64	5,249,576	10-1993	Goldberger et al.	
	65	5,297,548	03-1994	Pologe, Jonas A.	
	66	5,319,355	06-1994	Russek	
	67	5,362,966	11-1994	Rosenthal et al.	
	68	5,437,275	08-1995	Amundsen et al.	
	69	5,479,934	01-1996	Imran	
	70	5,482,034	01-1996	Lewis et al.	
	71	5,511,546	04-1996	Hon, Edward H.	
	72	5,534,851	07-1996	Russek	
	73	5,553,615	09-1996	Carim et al.	
	74	5,553,616	09-1996	Ham et al.	
	75	5,750,927	05-1998	Baltazar, Osni	
	76	5,752,914	05-1998	Delonzor et al.	
	77	5,792,052	08-1998	Isaacson et al.	
	78	5,826,885	10-1998	Helgeland	
	79	5,902,235	05-1999	Lewis et al.	
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	81	6,049,727	04-2000	Crothall, Katherine D.	
	82	6,128,521	10-2000	Marro et al.	
	83	6,129,675	10-2000	Jay	
	84	6,144,866	11-2000	Miesel et al.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English Language Translation is attached.



PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 4 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	85	6,181,958	01-2001	Steuer et al.	
	86	6,223,063	04-2001	Chaiken et al.	
	87	6,253,097	06-2001	Aronow et al.	
	88	6,301,493	10-2001	Marro et al.	
	89	6,317,627	11-2001	Ennen et al.	
	90	6,353,750	03-2002	Kimura et al.	
	91	6,360,113	03-2002	Dettling, Allen	
	92	6,430,437	08-2002	Marro	
	93	6,606,509	08-2003	Schmitt, Joseph M.	
	94	6,636,759	10-2003	Robinson, Mark Ries	
	95	7,254,429	08-2007	Schurman et al.	
	96	7,510,849	03-2009	Schurman et al.	
	97	7,356,365	04-2009	Schurman	
	98	7,657,294	02-2010	Eghbal et al.	
	99	7,657,295	02-2010	Coakley et al.	
	100	7,657,296	02-2010	Raridan et al.	
	101	7,729,733	06-2010	Al-Ali et al.	
	102	7,761,127	07-2010	Al-Ali et al.	
	103	7,761,128	07-2010	Al-Ali et al.	
	104	7,764,982	07-2010	Dalke et al.	
	105	7,791,155	09-2010	Diab	
	106	7,801,581	09-2010	Diab	
	107	7,822,452	10-2010	Schurman et al.	
	108	7,844,313	11-2010	Kiani et al.	
	109	7,844,314	11-2010	Al-Ali	
	110	7,844,315	11-2010	Al-Ali	
	111	7,865,222	01-2011	Weber et al.	
	112	7,873,497	01-2011	Weber et al.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English Language Translation is attached.

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 5 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	113	7,880,606	02-2011	Al-Ali	
	114	7,880,626	02-2011	Al-Ali et al.	
	115	7,891,355	02-2011	Al-Ali et al.	
	116	7,894,868	02-2011	Al-Ali et al.	
	117	7,899,507	03-2011	Al-Ali et al.	
	118	7,899,518	03-2011	Trepagnier et al.	
	119	7,904,132	03-2011	Weber et al.	
	120	7,909,772	03-2011	Popov et al.	
	121	7,910,875	03-2011	Al-Ali	
	122	7,919,713	04-2011	Al-Ali et al.	
	123	7,937,128	05-2011	Al-Ali	
	124	7,937,129	05-2011	Mason et al.	
	125	7,937,130	05-2011	Diab et al.	
	126	7,941,199	05-2011	Kiani	
	127	7,951,086	05-2011	Flaherty et al.	
	128	7,957,780	06-2011	Lamego et al.	
	129	7,962,188	06-2011	Kiani et al.	
	130	7,962,190	06-2011	Diab et al.	
	131	7,976,472	07-2011	Kiani	
	132	7,988,637	08-2011	Diab	
	133	7,990,382	08-2011	Kiani	
	134	7,991,446	08-2011	Al-Ali et al.	
	135	8,000,761	08-2011	Al-Ali	
	136	8,008,088	08-2011	Bellott et al.	
	137	8,019,400	09-2011	Diab et al.	
	138	8,028,701	10-2011	Al-Ali et al.	
	139	8,029,765	10-2011	Bellott et al.	
	140	8,036,728	10-2011	Diab et al.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English Language Translation is attached.

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
SHEET 6 OF 7	Attorney Docket No.	CERCA.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	141	8,046,040	10-2011	Ali et al.	
	142	8,046,041	10-2011	Diab et al.	
	143	8,046,042	10-2011	Diab et al.	
	144	8,048,040	11-2011	Kiani	
	145	8,050,728	11-2011	Al-Ali et al.	
	146	8,118,620	02-2012	Al-Ali et al.	
	147	8,126,528	02-2012	Diab et al.	
	148	8,128,572	03-2012	Diab et al.	
	149	8,130,105	03-2012	Al-Ali et al.	
	150	8,145,287	03-2012	Diab et al.	
	151	8,150,487	04-2012	Diab et al.	
	152	8,175,672	05-2012	Parker	
	153	8,180,420	05-2012	Diab et al.	
	154	8,182,443	05-2012	Kiani	
	155	8,185,180	05-2012	Diab et al.	
	156	8,190,223	05-2012	Al-Ali et al.	
	157	8,190,227	05-2012	Diab et al.	
	158	7,734,320	06-2012	Al-Ali	
	159	8,203,438	06-2012	Kiani et al.	
	160	8,203,704	06-2012	Merritt et al.	
	161	8,224,411	07-2012	Al-Ali et al.	
	162	8,228,181	07-2012	Al-Ali	
	163	8,229,533	07-2012	Diab et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>

NON PATENT LITERATURE DOCUMENTS
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Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English Language Translation is attached.

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>  SHEET 7 OF 7	Application No.	12/534827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze, et al.
	Art Unit	3777
	Examiner	Liu, Chu Chuan
	Attorney Docket No.	CERCA.002A

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	164	PCT International Search Report, App. No. PCT/US2010/047899, Date of Actual Completion of Search: 01/26/2011, 4 pages.	
	165	International Preliminary Report on Patentability and Written Opinion of the International Searching Authority issued in Application No. PCT US2009/049638, mailed January 5, 2011 in 9 pages.	
	166	<a href="http://www.masimo.com/rainbow/pronto.htm">http://www.masimo.com/rainbow/pronto.htm</a> Noninvasive & Immediate Hemoglobin Testing, printed on August 20, 2009	
	167	<a href="http://www.masimo.com/pulseOximeter/Rad5.htm">http://www.masimo.com/pulseOximeter/Rad5.htm</a> ; Signal Extraction Pulse Oximeter, printed on August 20, 2009	
	168	<a href="http://blogderoliveira.blogspot.com/2008_02_01_archive.html">http://blogderoliveira.blogspot.com/2008_02_01_archive.html</a> ; Ricardo Oliveira, printed on August 20, 2009	
	169	<a href="http://www.masimo.com/rad-57/">http://www.masimo.com/rad-57/</a> ; Noninvasive Measurement of Methemoglobin, Carboxyhemoglobin and Oxyhemoglobin in the blood. Printed on August 20, 2009	
	170	<a href="http://amivital.ugr.es/blog/?tag+spo2">http://amivital.ugr.es/blog/?tag+spo2</a> ; Monitorizacion de la hemoglobina...y mucho mas, printed on August 20, 2009	
	171	<a href="http://www.masimo.com/spco/">http://www.masimo.com/spco/</a> ; Carboxyhemoglobin Noninvasive > Continuous > Immediate, printed on August 20, 2009	
	172	<a href="http://www.masimo.com/PARTNERS/WELCHALLYN.htm">http://www.masimo.com/PARTNERS/WELCHALLYN.htm</a> ; Welch Allyn Expands Patient Monitor Capabilities with Masimo Pulse Oximetry Technology, printed on August 20, 2009	
	173	<a href="http://www.masimo.com/pulseOximeter/PPO.htm">http://www.masimo.com/pulseOximeter/PPO.htm</a> ; Masimo Personal Pulse Oximeter, printed on August 20, 2009	
	174	<a href="http://www.masimo.com/generalFloor/system.htm">http://www.masimo.com/generalFloor/system.htm</a> ; Masimo Patient SafetyNet System at a Glance, printed on August 20, 2009	
	175	<a href="http://www.masimo.com/partners/GRASEBY.htm">http://www.masimo.com/partners/GRASEBY.htm</a> ; Graseby Medical Limited, printed on August 20, 2009	
	176	International Search Report and Written Opinion for PCT/US2009/049638, mailed January 7, 2010.	

14447015

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English Language Translation is attached.

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

**PCT**


To:  
Altman, Daniel E.  
KNOBBE, MARTENS, OLSON & BEAR, LLP  
2040 Main Street, 14th Floor  
Irvine, CA 92614  
ETATS-UNIS D'AMERIQUE

**NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION**

(PCT Rule 44.1)

	Date of mailing (day/month/year)  26 January 2011 (26-01-2011)
Applicant's or agent's file reference MLHUM008VPC	<b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below
International application No. PCT/US2010/047899	International filing date (day/month/year)  3 September 2010 (03-09-2010)
Applicant  MASIMO LABORATORIES, INC.	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.
- Filing of amendments and statement under Article 19:**  
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):
- When?** The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report.
- Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70
- For more detailed instructions, see PCT Applicant's Guide, International Phase, paragraphs 9.004 - 9.011.**
2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. **Reminders**
- The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. Following the expiration of 30 months from the priority date, these comments will also be made available to the public.
- Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).
- Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.
- In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.
- For details about the applicable time limits, Office by Office, see [www.wipo.int/pct/en/texts/time\\_limits.html](http://www.wipo.int/pct/en/texts/time_limits.html) and the *PCT Applicant's Guide, National Chapters*.

Name and mailing address of the International Searching Authority   European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040 Fax: (+31-70) 340-3016	Authorized officer  THOMAS, Roger Tel: +49 (0)89 2399-2247
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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>MLHUM008VPC</b>	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. <b>PCT/US2010/047899</b>	International filing date (day/month/year) <b>03/09/2010</b>	(Earliest) Priority Date (day/month/year) <b>03/09/2009</b>
Applicant <b>MASIMO LABORATORIES, INC.</b>		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

- b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6b(a)).  
c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (see Box No. III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant  
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☐ the text is approved as submitted by the applicant  
☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 5  
☐ as suggested by the applicant  
☐ as selected by this Authority, because the applicant failed to suggest a figure  
☒ as selected by this Authority, because this figure better characterizes the invention  
b. ☐ none of the figures is to be published with the abstract

Form PCT/ISA/210 (first sheet) (July 2009)

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US2010/047899

**Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)**

Embodiments of the present disclosure include an emitter driver configured to be capable of addressing substantially  $2^N$  nodes with N cable conductors configured to carry activation instructions from a processor (402). In an embodiment, an address controller (502) outputs an activation instruction to a latch decoder (506) configured to supply switch controls to activate particular LEDs of a light source (418).

Form PCT/ISA/210 (continuation of first sheet (3)) (July 2009)

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2010/047899

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> INV. A61B5/00 A61B5/1455 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) A61B Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2009/163775 A1 (BARRETT BRUCE J [US] ET AL) 25 June 2009 (2009-06-25)	8-14
Y	paragraphs [0002], [0003], [0016] - [0018] paragraphs [0027] - [0039]; figures 6-10	1-7, 15
X	US 2007/165218 A1 (QING XINLIN [US] ET AL) 19 July 2007 (2007-07-19)	8-14
Y	paragraphs [0003], [0005] paragraphs [0028] - [0036]; figures 3-9	1-7, 15
A	US 2007/293792 A1 (SLIWA JOHN W [US] ET AL) 20 December 2007 (2007-12-20) paragraphs [0023], [0060]; figures	1, 8, 15
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
11 January 2011		26/01/2011
Name and mailing address of the ISA/ European Patent Office, P.B. 5618 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer  Rosenblatt, Thomas

Form PCT/ISA/210 (second sheet) (April 2005)



CX-1621

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No

PCT/US2010/047899

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2009163775 A1	25-06-2009	WO 2009085822 A1	09-07-2009
US 2007165218 A1	19-07-2007	NONE	
US 2007293792 A1	20-12-2007	NONE	

Form PCT/ISA/210 (patent family annex) (April 2005)

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

To:

see form PCT/ISA/220

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)Applicant's or agent's file reference  
see form PCT/ISA/220**FOR FURTHER ACTION**  
See paragraph 2 belowInternational application No.  
PCT/US2010/047899International filing date (day/month/year)  
03.09.2010Priority date (day/month/year)  
03.09.2009International Patent Classification (IPC) or both national classification and IPC  
INV. A61B5/00 A61B5/1455Applicant  
MASIMO LABORATORIES, INC.

## 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

## 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0  
Fax: +49 89 2399 - 4465

Date of completion of  
this opinion

see form  
PCT/ISA/210

Authorized Officer

Rosenblatt, Thomas  
Telephone No. +49 89 2399-8438



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2010/047899**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of:
  - ☒ the international application in the language in which it was filed
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:
  - a. (means)
    - ☐ on paper
    - ☐ in electronic form
  - b. (time)
    - ☐ in the international application as filed
    - ☐ together with the international application in electronic form
    - ☐ subsequently to this Authority for the purposes of search
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. Statement

Novelty (N)	Yes: Claims	<u>1-7, 11-13, 15</u>
	No: Claims	<u>8-10, 14</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-15</u>
Industrial applicability (IA)	Yes: Claims	<u>1-15</u>
	No: Claims	

## 2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2010/047899

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**Box No. VII Certain defects in the international application**

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The following defects in the form or contents of the international application have been noted:

see separate sheet

---

**Box No. VIII Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2010/047899

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

- 1 Reference is made to the following documents:  
D1: US-A-2009/0163775,  
D2: US-A-2007/0165218,  
D3: US-A-2007/0293792.
- 2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1 to 7 and 15 does not involve an inventive step in the sense of Article 33(3) PCT.
- 2.1 D1 is regarded as being the prior art closest to the subject-matter of claim 1, and discloses in Figure 6 in combination with Figures 7 to 11 a non-invasive physiological sensor (see paragraphs [0016,17]) configured to output one or more signals indicative of one or more physiological conditions of a patient being monitored, the sensor comprising:
  - a plurality of light emitting sources (18) configured for transmitting optical radiation to a measurement site;
  - one or more detectors (20,22) configured to output said one or more signals responsive to said optical radiation detected after attenuation by body tissue of said patient at said measurement site, said one or more signals indicative of said one or more physiological conditions of said patient.
- 2.2 The subject-matter of claim 1 therefore differs from this known sensor in that the sensor comprises a plurality of switches configured for selectively connecting one or more of the light emitting sources to one or more drive signals; and a decoder circuit (26) configured for controlling the plurality of switches, "wherein when said decoder circuit receives N inputs" (see also below item VIII) said decoder circuit configured to selectively address up to  $2^N$  unique locations, each location including one or more of said plurality of said semiconductor switches, wherein activation of one of said unique locations causes at least one of said light emitting sources to transmit said optical radiation to said measurement site.

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- 2.3 According to D1 the switches and decoder circuit are not comprised in the sensor but in an attached patient monitor and the number of unique locations to be addressed is  $N \cdot (N-1)/2$ , thus more limited (cf. paragraph [0018]). The problem to be solved may therefor be defined as increasing the number of switchable locations or light emitting sources to up to  $2^N$ , when using N sensor signal inputs.
- 2.4 The solution defined in claim 1 does not involve an inventive step for the following reasons.
- 2.4.1 It is preliminarily noted, that N is not limited in the claim, so that the claim covers also embodiments for  $N=1$  or  $N=2$ .
- 2.4.2 D2 discloses a similar sensor arrangement where an undefined number of monitoring elements (sensors, actuators, transducers, any type of sensor/ actuator may be used) shall be switched through a reduced number of control lines (304; 404; 704, 712; 804, 808; i.e.  $N=1$  or 2), which correspond to the N inputs according to claim 1. These control lines are bundled together with one or two signal lines into a cable (cf. end of paragraph [0036]) connecting the sensor to a controller. The sensor comprises switches (308, 408, 708, 716, 812, 908) which switch on or off thereto connected sensor/actuator elements. It is clear, that each of these switches inherently must comprise an actual switch and a decoder unit, which decoder unit is able to decode the control signal generated by the controller containing the information as to which of the monitoring elements is to be switched on or off (see for example paragraph [0029]). Hence D2 teaches in order to limit the number of wires in a cable for switching a great number of sensor elements to 1 or 2 wires (without limit to  $2^N$  sensor elements), to use an encoded control signal which is decoded in switches comprised in the sensor assembly, where each switch individually is activated depending on the control signal guided by the control line to the assembly, the switch of each sensor element implicitly comprising an actual switch element and a decoder unit. Hence, there is no "a decoder circuit for controlling the plurality of switches", rather a plurality of decoder circuits, and the number of sensor elements is not limited to  $2^N$ .
- 2.4.3 The skilled person entrusted with the solution of the above identified technical problem would consider D2, because it relates to the same problem in the same technical field, and, applying its teaching to the device of D1, would arrive at a sensor with a number of decoder units, driven over one or two control lines. It is clear to the skilled person, that in order to further reduce costs and complexity of the sensor assembly, which is a common constraint in R&D, in particular if a large number of sensor elements is to be controlled, the

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individual decoder units would need to be integrated in a single decoder unit/ circuit which would then address the individual switches of each sensor element. The use of a single decoder circuitry in such cases may be considered as state of the art (for example D3, end of paragraphs [0023] and [0060]) at the date of filing of the present application. It appears that the limitation to  $2^N$  sensor elements does not produce any particular technical effect and may only be considered as a constraint, which the skilled person would consider in the design of the sensor assembly if need is. There appears to be also no particular effect in the requirement of using N inputs controlling  $2^N$  sensor elements. Also this appears only to be an additional design constraint which does not appear to involve any difficulty to be implemented if need is. Consequently, the combination of the teaching of D2 with the sensor known from D1, and carrying out further modifications belonging to the normal practice of the skilled person, obviously leads to a sensor assembly which falls under the scope of claim 1.

- 2.5 Dependent claims 2 to 7 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, the reasons being as follows:
- 2.5.1 The additional features of the following claims are known from D1:  
claim 2: see Figure 1;  
claim 8: see Figure 7-8, symbols indicate to the skilled person LEDs.
- 2.5.2 Grouping of light emitting sources or sensor elements according to claim 5 is known from both D1 (Figures 9, 10, and corresponding passages) or D2 (Fig. 9), using different drive signals according to claim 6 at least from D1, Figure 10).
- 2.5.3 Consequently none of the additional features of these claims changes the finding presented under 2.4.
- 2.5.4 In claims 3 and 4 slight constructional changes in the sensor of claim 1 are defined which come within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Consequently, the subject-matter of these claims also lacks an inventive step.
- 2.6 The method according to claim 15 is implicitly carried out, when using a sensor according to claim 1. It consequently lacks inventive step for equivalent reasons as set out above for the subject-matter of claim 1.

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- 3 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 8-10 and 14 is not new in the sense of Article 33(2) PCT.
- 3.1 Claim 8 is directed to a cable comprising as structural technical features only one or more signal lines and N address lines (see also item VIII below). The remaining functional features defined in the claim ("configured to carry...", "capable of selecting...") do not impose any further structural limitation on the cable itself. The cables known from D1 and D2 are suitable to be used for the same functions. Consequently the subject-matter of claim 8 is not new.
- 3.2 The cable used in Figures 7 and 8 of D2 comprises two signal lines. The cable is consequently anticipating the additional structural features of claims 9 and 10; the remaining functional statements in these claims do not limit the cable any further, so that also claims 9 and 10 lack novelty.
- 3.3 The additional features of claim 14 are no features of the actual cable, the cables known from D1 and D2 are suitable to be used for the functional definition of the claim, so that also this claim lacks novelty.
- 4 In claims 11 to 13 slight constructional changes in the cable of claim 8 are defined which come within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. In particular the provision of input and output connectors and flexible conduits belongs to the common knowledge of the skilled person. Integrating the decoder circuit in the cable, in particular in the output connector, also does not produce any unexpected technical effect. Consequently, the subject-matter of these claims lacks an inventive step (Article 33 (3) PCT).

**Re Item VII****Certain defects in the international application**

- 5 The independent claims are not drafted in two-part form, contrary to Rule 6.3b) PCT.
- 6 The claims are not provided with reference signs, contrary to Rule 6.2b) PCT.



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**Re Item VIII**

**Certain observations on the international application**

- 7 The claims do not meet the requirement of Article 6 PCT, in that their subject-matter lacks clarity.
- 7.1 In claim 1 reference is made to "said semiconductor switches", whereas only a plurality of switches had been defined before. A doubt arises whether the same switches are meant.
- 7.2 The feature "wherein when said decoder circuit receives N inputs" is ambiguous. The term "input" may be understood as referring to a signal or to a physical entry. This ambiguity is confirmed when looking to claim 2, according to which input should be understood as referring to a signal. The above statement leaves it unclear whether the decoder has a single physical input, in the sense of an entry point, or N inputs. A single input may receive N input signals sequentially. However the description discloses decoder circuits only with N physical inputs, no sequential transmission is envisaged. The claim needs clarification.
- 7.3 Claim 8 relates to a cable and its signal and address lines. It comprises a number of functional definitions which do not clearly limit the structure of the claim. At least it is not clear whether the additional functional features of the N address lines "capable of selecting...", "configured to selectively...", and "thereby activating..." can be a limitation of the cable. It appears that these features are functions of a decoder circuit and not of a cable. At present these functional statements are not considered as structurally limiting the cable. Similar objections also apply to claims 9,10 and 14.

Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO-ISA)

General information	For all international applications filed on or after 01/01/2004 the competent ISA will establish an ISR. It is accompanied by the WO-ISA. Unlike the former written opinion of the IPEA (Rule 66.2 PCT), the WO-ISA is not meant to be responded to, but to be taken into consideration for further procedural steps. This document explains about the possibilities.
Amending claims under Art. 19 PCT	Within 2 months after the date of mailing of the ISR and the WO-ISA the applicant may file amended claims under Art. 19 PCT directly with the International Bureau of WIPO. The PCT reform of 2004 did not change this procedure. For further information please see Rule 46 PCT as well as form PCT/ISA/220 and the corresponding Notes to form PCT/ISA/220.
Filing a demand for international preliminary examination	<p>In principle, the WO-ISA will be considered as the written opinion of the IPEA. This should, in many cases, make it unnecessary to file a demand for international preliminary examination. If the applicant nevertheless wishes to file a demand this must be done before expiry of 3 months after the date of mailing of the ISR/ WO-ISA or 22 months after priority date, whichever expires later (Rule 54bis PCT). Amendments under Art. 34 PCT can be filed with the IPEA as before, normally at the same time as filing the demand (Rule 66.1 (b) PCT).</p> <p>If a demand for international preliminary examination is filed and no comments/amendments have been received the WO-ISA will be transformed by the IPEA into an IPRP (International Preliminary Report on Patentability) which would merely reflect the content of the WO-ISA. The demand can still be withdrawn (Art. 37 PCT).</p>
Filing informal comments	After receipt of the ISR/WO-ISA the applicant may file informal comments on the WO-ISA directly with the International Bureau of WIPO. These will be communicated to the designated Offices together with the IPRP (International Preliminary Report on Patentability) at 30 months from the priority date. Please also refer to the next box.
End of the international phase	At the end of the international phase the International Bureau of WIPO will transform the WO-ISA or, if a demand was filed, the written opinion of the IPEA into the IPRP, which will then be transmitted together with possible informal comments to the designated Offices. The IPRP replaces the former IPEA (international preliminary examination report).
Relevant PCT Rules and more information	Rule 43 PCT, Rule 43bis PCT, Rule 44 PCT, Rule 44bis PCT, PCT Newsletter 12/2003, OJ 11/2003, OJ 12/2003

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference MLHUM.007VPC	<b>FOR FURTHER ACTION</b> See item 4 below	
International application No. PCT/US2009/049638	International filing date ( <i>day/month/year</i> ) 02 July 2009 (02.07.2009)	Priority date ( <i>day/month/year</i> ) 03 July 2008 (03.07.2008)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant MASIMO LABORATORIES, INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input checked="" type="checkbox"/> | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70		Date of issuance of this report 05 January 2011 (05.01.2011)
Form PCT/IB/373 (January 2004)		Authorized officer <b>Athina Nickitas-Etienne</b> e-mail: pt04.pct@wipo.int

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)Applicant's or agent's file reference  
see form PCT/ISA/220**FOR FURTHER ACTION**  
See paragraph 2 belowInternational application No.  
PCT/US2009/049638International filing date (day/month/year)  
02.07.2009Priority date (day/month/year)  
03.07.2008International Patent Classification (IPC) or both national classification and IPC  
INV. A61B5/00Applicant  
MASIMO LABORATORIES, INC.

## 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

## 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office  
P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040  
Fax: +31 70 340 - 3016

Date of completion of  
this opinion

see form  
PCT/ISA/210

Authorized Officer

Ferrigno, Antonio

Telephone No. +31 70 340-2174



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of:
  - ☒ the international application in the language in which it was filed
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ on paper
    - ☐ in electronic form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in electronic form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. **Additional comments:**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/049638**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 22-53

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for the whole application or for said claims Nos. 22-53

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/049638**Box No. IV Lack of unity of invention**

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☐ paid additional fees
  - ☐ paid additional fees under protest and, where applicable, the protest fee
  - ☐ paid additional fees under protest but the applicable protest fee was not paid
  - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
  - ☒ not complied with for the following reasons:  
**see separate sheet**
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
  - ☒ the parts relating to claims Nos. 1-21

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. Statement

Novelty (N)	Yes: Claims	<u>3-8</u>
	No: Claims	<u>1,2,9-21</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-21</u>
Industrial applicability (IA)	Yes: Claims	<u>1-21</u>
	No: Claims	

## 2. Citations and explanations

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

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**Re Item III.**

Claims 22-53 not searched: see **Re Item IV** below.

**Re Item IV.**

The separate inventions/groups of inventions are:

1-21

physiological sensor with means to reduce thickness of body tissue

22-31

physiological sensor with a heat sink

32-38

heat sink of a medical sensor

39-46

conductive shield for a light sensitive detector

47-53

optical sensor comprising a noise shield

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

Document US2006/0211924 discloses (cf passages cited in the search report) the common features of claims 1 and 15. The remaining features are a bump as recited in claim 1, and a partially cylindrical lens as recited in claim 15. These features solve the problem of reducing thickness of body tissue and can be considered the first invention.

The subject-matter of claim 22 differs from the disclosure of document US2006/0211924 in that a heat sink is provided as recited in claim 22. This feature solves the problem of cooling the optical source and can be considered a second different invention.

The subject-matter of claim 32 is directed to an heat sink and doesn't have any feature in common with claims 1 and 15. It also doesn't have any feature in common with the subject-matter of claim 22, other than a "heat sink" (which is generally a known device). It solves the problem of providing an efficient heat sink and therefore can be



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considered a third different invention.

The subject-matter of claim 39 is directed to a conductive shield and doesn't have any feature in common with claims 1, 15, 22 and 32. It solves the problem of providing an efficient noise shielding device and therefore can be considered a fourth different invention.

Document US2006/0211924 discloses (cf passages cited in the search report) the common features of claims 1, 15, 22. and 47. Claim 47 provides the extra feature of a conductive shield. Claim 47 doesn't have any feature in common with claim 32. It also doesn't have any feature in common with claim 39, other than a "conductive shield" (which is generally a known device). The conductive shield, as recited in claim 47, solves the problem of protecting the sensor from noise interference and therefore can be considered a fifth different invention.

**Re Item V.**

1 Reference is made to the following documents:

- D1: US 2004/054291 A1 (SCHULZ CHRISTIAN [US] ET AL) 18 March 2004 (2004-03-18)
- D2: US-B1-6 345 194 (NELSON ROBERT S [US] ET AL) 5 February 2002 (2002-02-05)
- D3: WO 93/12712 A (VIVASCAN CORP [US]) 8 July 1993 (1993-07-08)

2 INDEPENDENT CLAIM 1

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.

Document D1 discloses (the references in parentheses applying to this document):

a noninvasive physiological sensor (1900, cf. paragraph 65 and figures 19A-D) for

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

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measuring one or more physiological parameters of a medical patient, the sensor comprising:

a light source (not shown in these figure; cf. paragraph 35 and claim 1);  
a photodetector (not shown in these figure; cf. paragraph 35 and claim 1) operative to detect light from said light source after attenuation by body tissue of a medical patient and to generate a physiological signal responsive to the detected light, the physiological signal reflecting one or more physiological parameters of the medical patient (cf. paragraph 3); and  
a bump (1920,1921) interposed between the light source and the photodetector, the bump protruding from a tissue contacting surface, the bump configured to reduce a thickness of the body tissue between the light source and the photodetector such that an optical pathlength between the light source and the photodetector is reduced (see spring 1910).

Hence, the subject-matter of claim 1 is disclosed in document D1.

2.2 The subject-matter of claim 1 is also disclosed in documents D2 and D3 (see corresponding passages cited in the search report: although the device disclosed in D2 is used for image mammography, it is also suitable to be used with other processing devices, and therefore for measuring one or more physiological parameters of a medical patient).

### 3 INDEPENDENT CLAIM 15

3.1 The bumps (1920,1921) disclosed in document D1 are partially cylindrical lenses (see paragraph 68). Hence, the same reasoning applies, mutatis mutandis, to the subject-matter of independent claim 15, which therefore is also considered not new.

### 4 DEPENDENT CLAIMS 2-14, 16-21

4.1 For the same reasons also the subject-matter of dependent claim 2 is considered not new.

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- 4.2 The additional features of dependent claims 9, 10, 18-21 attempt to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result (Article 6 PCT). However these features appear to be disclosed in document D1 (see passages cited in the search report). Hence, also the subject-matter of these claims is considered not new.
- 4.3 The additional features of dependent claims 11-14, 16, and 17 are also disclosed in document D1 (see passages cited in the search report). Hence, also the subject-matter of these claims is considered not new.
- 4.4 The additional features of dependent claims 3-8 are just some dimensional straightforward possibilities which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill (Articles 33(1) and 33(3) PCT).

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

**PCT**


<b>To:</b> KNOBBE, MARTENS, OLSON Attn: Altman, Daniel E. AND BEAR, LLP 2040 Main Street, Fourteenth Floor Irvine, CA 92614 ETATS-UNIS D'AMERIQUE
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NOTIFICATION OF TRANSMITTAL OF  
 THE INTERNATIONAL SEARCH REPORT AND  
 THE WRITTEN OPINION OF THE INTERNATIONAL  
 SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing (day/month/year) 07/01/2010	
Applicant's or agent's file reference MLHUM.007VPC	<b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below
International application No. PCT/US2009/049638	International filing date (day/month/year) 02/07/2009
Applicant MASIMO LABORATORIES, INC.	

1. <input checked="" type="checkbox"/> The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith. <b>Filing of amendments and statement under Article 19:</b> The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46): <b>When?</b> The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report. <b>Where?</b> Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70 <b>For more detailed instructions, see the notes on the accompanying sheet.</b>
2. <input type="checkbox"/> The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. <input type="checkbox"/> <b>With regard to any protest</b> against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that: <input type="checkbox"/> the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices. <input type="checkbox"/> no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
<b>4. Reminders</b> Shortly after the expiration of <b>18 months</b> from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication. The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date. Within <b>19 months</b> from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase <b>until 30 months</b> from the priority date (in some Offices even later); otherwise, the applicant must, <b>within 20 months</b> from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices. In respect of other designated Offices, the time limit of <b>30 months</b> (or later) will apply even if no demand is filed within 19 months. See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the <i>PCT Applicant's Guide</i> , National Chapters.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Lars-Oliver Römich
--	--

**NOTES TO FORM PCT/ISA/220**

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

**INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19**

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annex B).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, International Phase, paragraph 296).

**What parts of the international application may be amended?**

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

**When?**

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

**Where not to file the amendments?**

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

**How?**

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet or sheets containing a complete set of claims in replacement of all the claims previously filed must be submitted.

Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively in Arabic numerals (Section 205(a)).

**The amendments must be made in the language in which the international application is to be published.**

**What documents must/may accompany the amendments?****Letter (Section 205(b)):**

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.**

**NOTES TO FORM PCT/ISA/220**

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

**INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19**

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annex B).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, International Phase, paragraph 296).

**What parts of the international application may be amended?**

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

**When?**

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

**Where not to file the amendments?**

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

**How?**

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet or sheets containing a complete set of claims in replacement of all the claims previously filed must be submitted.

Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively in Arabic numerals (Section 205(a)).

**The amendments must be made in the language in which the international application is to be published.**

**What documents must/may accompany the amendments?****Letter (Section 205(b)):**

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.**

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>MLHUM.007VPC</b>	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. <b>PCT/US2009/049638</b>	International filing date (day/month/year) <b>02/07/2009</b>	(Earliest) Priority Date (day/month/year) <b>03/07/2008</b>
Applicant <b>MASIMO LABORATORIES, INC.</b>		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant  
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant  
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. 2B

- ☒ as suggested by the applicant  
☐ as selected by this Authority, because the applicant failed to suggest a figure  
☐ as selected by this Authority, because this figure better characterizes the invention

b. ☐ none of the figures is to be published with the abstract

## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2009/049638

**A. CLASSIFICATION OF SUBJECT MATTER**  
INV. A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/054291 A1 (SCHULZ CHRISTIAN [US] ET AL) 18 March 2004 (2004-03-18) paragraphs [0003], [0007], [0036], [0037], [0042], [0065] - [0068]	1-21
X	US 6 345 194 B1 (NELSON ROBERT S [US] ET AL) 5 February 2002 (2002-02-05) abstract column 1, line 31 - column 2, line 9 column 3, lines 14-23 column 9, line 63 - column 10, line 44 column 11, lines 36-58 column 13, lines 15-40 ----- -/--	1



Further documents are listed in the continuation of Box C.



See patent family annex.

## \* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

21 September 2009

Date of mailing of the international search report

07/01/2010

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040.  
Fax: (+31-70) 340-3016

Authorized officer

Ferrigno, Antonio

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Form PCT/ISA/210 (second sheet) (April 2005)



CX-1621

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2009/049638

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93/12712 A (VIVASCAN CORP [US]) 8 July 1993 (1993-07-08) abstract page 6, line 22 - page 7, line 25 page 10, line 11 - page 11, line 3	1
A	US 6 360 115 B1 (GREENWALD ROGER J [US] ET AL) 19 March 2002 (2002-03-19) abstract column 2, line 49 - column 3, line 37	1,10,13
A	US 2006/211924 A1 (DALKE DAVID [US] ET AL) 21 September 2006 (2006-09-21) cited in the application abstract paragraphs [0007], [0064]	1,15

3

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2009/049638**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-21

**Remark on Protest**

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

International Application No. PCT/US2009 /049638

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-21

physiological sensor with means to reduce thickness of body tissue  
---

2. claims: 22-31

physiological sensor with a heat sink  
---

3. claims: 32-38

heat sink of a medical sensor  
---

4. claims: 39-46

conductive shield for a light sensitive detector  
---

5. claims: 47-53

optical sensor comprising a noise shield  
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CX-1621

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No

PCT/US2009/049638

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004054291	A1	18-03-2004	NONE
US 6345194	B1	05-02-2002	NONE
WO 9312712	A	08-07-1993	AU 2245092 A 28-07-1993 JP 2637344 B2 06-08-1997 JP 6290307 A 18-10-1994 US 5372135 A 13-12-1994
US 6360115	B1	19-03-2002	AU 8908798 A 08-03-1999 EP 1005288 A1 07-06-2000 WO 9908588 A1 25-02-1999 US 5978695 A 02-11-1999
US 2006211924	A1	21-09-2006	EP 1860989 A1 05-12-2007 EP 1860990 A1 05-12-2007 EP 1860991 A1 05-12-2007 EP 1860992 A1 05-12-2007 EP 1863380 A2 12-12-2007 EP 1860993 A1 05-12-2007 EP 1860994 A1 05-12-2007 EP 1860995 A1 05-12-2007 EP 1860996 A1 05-12-2007 EP 1895892 A1 12-03-2008 EP 1860997 A1 05-12-2007 JP 2008531211 T 14-08-2008 JP 2008531212 T 14-08-2008 JP 2008535540 T 04-09-2008 JP 2008531214 T 14-08-2008 JP 2008531215 T 14-08-2008 JP 2008532589 T 21-08-2008 JP 2008538186 T 16-10-2008 JP 2008531216 T 14-08-2008 JP 2008531217 T 14-08-2008 JP 2008531218 T 14-08-2008 JP 2008531225 T 14-08-2008 US 2008220633 A1 11-09-2008 US 2006220881 A1 05-10-2006 US 2006211922 A1 21-09-2006 US 2006241358 A1 26-10-2006 US 2006229509 A1 12-10-2006 US 2006211923 A1 21-09-2006 US 2006241363 A1 26-10-2006 US 2006238358 A1 26-10-2006 US 2006226992 A1 12-10-2006 US 2006211925 A1 21-09-2006 US 2006211932 A1 21-09-2006 WO 2006094107 A1 08-09-2006 WO 2006094108 A1 08-09-2006 WO 2006094109 A1 08-09-2006 WO 2006094155 A1 08-09-2006 WO 2006115580 A2 02-11-2006 WO 2006094168 A1 08-09-2006 WO 2006094169 A1 08-09-2006 WO 2006094170 A1 08-09-2006 WO 2006094171 A1 08-09-2006 WO 2006118654 A1 09-11-2006 WO 2006094279 A1 08-09-2006

Form PCT/SA/210 (patent family annex) (April 2005)

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)Applicant's or agent's file reference  
see form PCT/ISA/220**FOR FURTHER ACTION**  
See paragraph 2 belowInternational application No.  
PCT/US2009/049638International filing date (day/month/year)  
02.07.2009Priority date (day/month/year)  
03.07.2008International Patent Classification (IPC) or both national classification and IPC  
INV. A61B5/00Applicant  
MASIMO LABORATORIES, INC.

## 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1b/s(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

## 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office  
P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040  
Fax: +31 70 340 - 3016

Date of completion of  
this opinionsee form  
PCT/ISA/210

Authorized Officer

Ferrigno, Antonio

Telephone No. +31 70 340-2174



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/049638

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**Box No. I Basis of the opinion**

---

1. With regard to the **language**, this opinion has been established on the basis of:
  - ☒ the international application in the language in which it was filed
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ on paper
    - ☐ in electronic form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in electronic form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/049638**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 22-53

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for the whole application or for said claims Nos. 22-53

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/049638**Box No. IV Lack of unity of invention**

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☐ paid additional fees
  - ☐ paid additional fees under protest and, where applicable, the protest fee
  - ☐ paid additional fees under protest but the applicable protest fee was not paid
  - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
  - ☒ not complied with for the following reasons:  
**see separate sheet**
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
  - ☒ the parts relating to claims Nos. 1-21

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. Statement

Novelty (N)	Yes: Claims	<u>3-8</u>
	No: Claims	<u>1,2,9-21</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-21</u>
Industrial applicability (IA)	Yes: Claims	<u>1-21</u>
	No: Claims	

## 2. Citations and explanations

**see separate sheet**



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/049638

**Re Item III.**

Claims 22-53 not searched: see **Re Item IV** below.

**Re Item IV.**

The separate inventions/groups of inventions are:

1-21

physiological sensor with means to reduce thickness of body tissue

22-31

physiological sensor with a heat sink

32-38

heat sink of a medical sensor

39-46

conductive shield for a light sensitive detector

47-53

optical sensor comprising a noise shield

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

Document US2006/0211924 discloses (cf passages cited in the search report) the common features of claims 1 and 15. The remaining features are a bump as recited in claim 1, and a partially cylindrical lens as recited in claim 15. These features solve the problem of reducing thickness of body tissue and can be considered the first invention.

The subject-matter of claim 22 differs from the disclosure of document US2006/0211924 in that a heat sink is provided as recited in claim 22. This feature solves the problem of cooling the optical source and can be considered a second different invention.

The subject-matter of claim 32 is directed to an heat sink and doesn't have any feature in common with claims 1 and 15. It also doesn't have any feature in common with the subject-matter of claim 22, other than a "heat sink" (which is generally a known device). It solves the problem of providing an efficient heat sink and therefore can be

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/049638

considered a third different invention.

The subject-matter of claim 39 is directed to a conductive shield and doesn't have any feature in common with claims 1, 15, 22 and 32. It solves the problem of providing an efficient noise shielding device and therefore can be considered a fourth different invention.

Document US2006/0211924 discloses (cf passages cited in the search report) the common features of claims 1, 15, 22, and 47. Claim 47 provides the extra feature of a conductive shield. Claim 47 doesn't have any feature in common with claim 32. It also doesn't have any feature in common with claim 39, other than a "conductive shield" (which is generally a known device). The conductive shield, as recited in claim 47, solves the problem of protecting the sensor from noise interference and therefore can be considered a fifth different invention.

**Re Item V.**

1 Reference is made to the following documents:

- D1: US 2004/054291 A1 (SCHULZ CHRISTIAN [US] ET AL) 18 March 2004  
(2004-03-18)
- D2: US-B1-6 345 194 (NELSON ROBERT S [US] ET AL) 5 February 2002  
(2002-02-05)
- D3: WO 93/12712 A (VIVASCAN CORP [US]) 8 July 1993 (1993-07-08)

2 INDEPENDENT CLAIM 1

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.

Document D1 discloses (the references in parentheses applying to this document):

a noninvasive physiological sensor (1900, cf. paragraph 65 and figures 19A-D) for

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/049638

measuring one or more physiological parameters of a medical patient, the sensor comprising:

- a light source (not shown in these figure; cf. paragraph 35 and claim 1);
- a photodetector (not shown in these figure; cf. paragraph 35 and claim 1) operative to detect light from said light source after attenuation by body tissue of a medical patient and to generate a physiological signal responsive to the detected light, the physiological signal reflecting one or more physiological parameters of the medical patient (cf. paragraph 3); and
- a bump (1920,1921) interposed between the light source and the photodetector, the bump protruding from a tissue contacting surface, the bump configured to reduce a thickness of the body tissue between the light source and the photodetector such that an optical pathlength between the light source and the photodetector is reduced (see spring 1910).

Hence, the subject-matter of claim 1 is disclosed in document D1.

- 2.2 The subject-matter of claim 1 is also disclosed in documents D2 and D3 (see corresponding passages cited in the search report: although the device disclosed in D2 is used for image mammography, it is also suitable to be used with other processing devices, and therefore for measuring one or more physiological parameters of a medical patient).

### 3 INDEPENDENT CLAIM 15

- 3.1 The bumps (1920,1921) disclosed in document D1 are partially cylindrical lenses (see paragraph 68). Hence, the same reasoning applies, mutatis mutandis, to the subject-matter of independent claim 15, which therefore is also considered not new.

### 4 DEPENDENT CLAIMS 2-14, 16-21

- 4.1 For the same reasons also the subject-matter of dependent claim 2 is considered not new.

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INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

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- 4.2 The additional features of dependent claims 9, 10, 18-21 attempt to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result (Article 6 PCT). However these features appear to be disclosed in document D1 (see passages cited in the search report). Hence, also the subject-matter of these claims is considered not new.
- 4.3 The additional features of dependent claims 11-14, 16, and 17 are also disclosed in document D1 (see passages cited in the search report). Hence, also the subject-matter of these claims is considered not new.
- 4.4 The additional features of dependent claims 3-8 are just some dimensional straightforward possibilities which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill (Articles 33(1) and 33(3) PCT).

**Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO-ISA)**

General information	For all international applications filed on or after 01/01/2004 the competent ISA will establish an ISR. It is accompanied by the WO-ISA. Unlike the former written opinion of the IPEA (Rule 66.2 PCT), the WO-ISA is not meant to be responded to, but to be taken into consideration for further procedural steps. This document explains about the possibilities.
Amending claims under Art. 19 PCT	Within 2 months after the date of mailing of the ISR and the WO-ISA the applicant may file amended claims under Art. 19 PCT directly with the International Bureau of WIPO. The PCT reform of 2004 did not change this procedure. For further information please see Rule 46 PCT as well as form PCT/ISA/220 and the corresponding Notes to form PCT/ISA/220.
Filing a demand for international preliminary examination	<p>In principle, the WO-ISA will be considered as the written opinion of the IPEA. This should, in many cases, make it unnecessary to file a demand for international preliminary examination. If the applicant nevertheless wishes to file a demand this must be done before expiry of 3 months after the date of mailing of the ISR/ WO-ISA or 22 months after priority date, whichever expires later (Rule 54bis PCT). Amendments under Art. 34 PCT can be filed with the IPEA as before, normally at the same time as filing the demand (Rule 66.1 (b) PCT).</p> <p>If a demand for international preliminary examination is filed and no comments/amendments have been received the WO-ISA will be transformed by the IPEA into an IPRP (International Preliminary Report on Patentability) which would merely reflect the content of the WO-ISA. The demand can still be withdrawn (Art. 37 PCT).</p>
Filing informal comments	After receipt of the ISR/WO-ISA the applicant may file informal comments on the WO-ISA directly with the International Bureau of WIPO. These will be communicated to the designated Offices together with the IPRP (International Preliminary Report on Patentability) at 30 months from the priority date. Please also refer to the next box.
End of the international phase	At the end of the international phase the International Bureau of WIPO will transform the WO-ISA or, if a demand was filed, the written opinion of the IPEA into the IPRP, which will then be transmitted together with possible informal comments to the designated Offices. The IPRP replaces the former IPER (international preliminary examination report).
Relevant PCT Rules and more information	Rule 43 PCT, Rule 43bis PCT, Rule 44 PCT, Rule 44bis PCT, PCT Newsletter 12/2003, OJ 11/2003, OJ 12/2003

Electronic Patent Application Fee Transmittal				
<b>Application Number:</b>	12534827			
<b>Filing Date:</b>	03-Aug-2009			
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze			
<b>Filer:</b>	Scott Edward Raevsky/Khylo Rhoden			
<b>Attorney Docket Number:</b>	CERCA.002A			
Filed as Large Entity				
<b>Utility under 35 USC 111(a) Filing Fees</b>				
<b>Description</b>	<b>Fee Code</b>	<b>Quantity</b>	<b>Amount</b>	<b>Sub-Total in USD(\$)</b>
<b>Basic Filing:</b>				
<b>Pages:</b>				
<b>Claims:</b>				
<b>Miscellaneous-Filing:</b>				
<b>Petition:</b>				
<b>Patent-Appeals-and-Interference:</b>				
<b>Post-Allowance-and-Post-Issuance:</b>				
<b>Extension-of-Time:</b>				

CX-1621

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
<b>Miscellaneous:</b>				
Submission- Information Disclosure Stmt	1806	1	180	180
<b>Total in USD (\$)</b>				<b>180</b>

CX-1621

<b>Electronic Acknowledgement Receipt</b>	
<b>EFS ID:</b>	14997124
<b>Application Number:</b>	12534827
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	1308
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	20995
<b>Filer:</b>	Scott Edward Raevsky/ADRIANA PEREZ
<b>Filer Authorized By:</b>	Scott Edward Raevsky
<b>Attorney Docket Number:</b>	CERCA.002A
<b>Receipt Date:</b>	20-FEB-2013
<b>Filing Date:</b>	03-AUG-2009
<b>Time Stamp:</b>	18:38:17
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$180
RAM confirmation Number	9249
Deposit Account	111410
Authorized User	KNOBBE MARTENS OLSON AND BEAR
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)</p>	

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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		002AIDS.pdf	308967	yes	8
			9e7c2b15499d5f0019a6867ece13488f09ed833b		
	Multipart Description/PDF files in .zip description				
	Document Description	Start	End		
	Transmittal Letter	1	1		
	Information Disclosure Statement (IDS) Form (SB08)	2	8		
Warnings:					
Information:					
2	Non Patent Literature	ISRWO.pdf	991771	no	14
			f20a76e6299702e90cf3caa4d3b27389260f9869		
Warnings:					
Information:					
3	Non Patent Literature	IPRP.pdf	352211	no	9
			0668b9fdb5823d123918611f8bed947951af79306		
Warnings:					
Information:					
4	Non Patent Literature	PRONTO.pdf	1063205	no	2
			71c5388012a1e926623305412da231428b3f3081		
Warnings:					
Information:					
5	Non Patent Literature	Rad5.pdf	609883	no	2
			65e1a14b509b63d5a0b54a0d594cb6160f6226e7		
Warnings:					
Information:					
6	Non Patent Literature	OLIVEIRA.pdf	6827165	no	8
			2de3999c0ffcecb5a66e73f718f87a21fcb22dcd		
Warnings:					
Information:					
7	Non Patent Literature	RAD57.pdf	1350450	no	3
			64468f9ea386fb67e7b56b44c44b5368f0a5a587		
Warnings:					
Information:					

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8	Non Patent Literature	SPO2.pdf	515558	no	2
			2c9d5954cbd26cf0c324b7877c50170ce788ddd3		
Warnings:					
Information:					
9	Non Patent Literature	SPCO.pdf	1209301	no	2
			4326023d9c403e1ac3e9d34e4f83e31c0ee1f8b		
Warnings:					
Information:					
10	Non Patent Literature	WELCH.pdf	678258	no	2
			86f8d5c5c61acff7f02cb208e5a56dcc8d1342ef		
Warnings:					
Information:					
11	Non Patent Literature	PPO.pdf	516438	no	1
			e5ca59b34109a5fe7023a6644b99ff91f097b95c		
Warnings:					
Information:					
12	Non Patent Literature	SAFETYNET.pdf	2165479	no	2
			b0aa2a782ed715e5cbd37a61ed893a954bb71959		
Warnings:					
Information:					
13	Non Patent Literature	GRASEBY.pdf	483484	no	1
			4bc584ce2c94c46a0b2c8c39e41ca14578d3af61		
Warnings:					
Information:					
14	Non Patent Literature	ISR2010.pdf	1263615	no	18
			459c31d02facc9c9ec76761e4ecfbd84474bfd3		
Warnings:					
Information:					
15	Fee Worksheet (SB06)	fee-info.pdf	30776	no	2
			26cc7b96a52c0da65a1e3dcf43f9f1f91c0338d3		
Warnings:					
Information:					
Total Files Size (in bytes):			18366561		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Docket No.: CERCA.002A

Customer No. 20995

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**INFORMATION DISCLOSURE STATEMENT**

Inventor	:	Jeroen Poeze, et al.
App. No.	:	12/534827
Filed	:	August 3, 2009
For	:	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
Examiner	:	Liu, Chu Chuan
Art Unit	:	3777
Conf. No.	:	1308

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Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**References and Listing**

Submitted herewith in the above-identified application is an Information Disclosure Statement listing references for consideration. Copies of any listed foreign and non-patent literature references are being submitted.

**Timing of Disclosure**

This Information Disclosure Statement is being filed after receipt of a first office action, but before the mailing date of a final action and before the mailing date of a Notice of Allowance. This Statement is accompanied by the fees set forth in 37 C.F.R. § 1.17(p). The Commissioner is hereby authorized to charge any additional fees which may be required or to credit any overpayment to Account No. 11-1410.

Respectfully submitted,  
KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: February 20, 2013

By: /Scott Raevsky/  
Scott Raevsky, Reg. No. 54,384  
Attorney of Record  
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(949) 721-7602

14447203

CX-1621



## UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/534,827	08/03/2009	Jeroen Poeze	CERCA.002A	1308

20995	7590	10/01/2012
KNOBBE MARTENS OLSON & BEAR LLP		
2040 MAIN STREET		
FOURTEENTH FLOOR		
IRVINE, CA 92614		

EXAMINER	
LIU, CHU CHUAN	

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
10/01/2012	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jayna.cartee@knobbe.com  
 efiling@knobbe.com

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>		
	12/534,827		POEZE ET AL.		
	<b>Examiner</b>		<b>Art Unit</b>		
CHU CHUAN (JJ) LIU		3777			

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on 03 August 2009.

2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

5) ☒ Claim(s) 1-34 is/are pending in the application.

5a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.

6) ☐ Claim(s) \_\_\_\_ is/are allowed.

7) ☒ Claim(s) 1-34 is/are rejected.

8) ☐ Claim(s) \_\_\_\_ is/are objected to.

9) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

10) ☐ The specification is objected to by the Examiner.

11) ☒ The drawing(s) filed on 03 August 2009 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>04/06/2010, 08/11/2010, 10/25/2011</u> .	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. ____. 5) <input type="checkbox"/> Notice of Informal Patent Application 6) <input type="checkbox"/> Other: _____.
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## **DETAILED ACTION**

### ***Claim Objections***

1. Claims 1, 11 and 16 are objected to because of the following informalities: In regard to claim 1, line 7, “output” should be set forth “outputs”. In regard to claims 11 and 16, “claim 6” should be set forth “claim 8”. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 102***

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-7 and 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Clarke et al. (USPN 5,222,496). In regard to claim 1, Clarke discloses a noninvasive device capable of producing a signal responsive to light attenuated by tissue at a measurement site (Figs. 1 and 2), the device comprising: an optical source configured to emit optical radiation (elements 12a-f, Fig. 2) at least at wavelengths between about 1600 nm and about 1700 nm (Col 3 lines 28-40); and a plurality of photodetectors each configured to detect the optical radiation from said optical source after attenuation by said tissue of said measurement site (elements 14 and 14a-f, Figs. 1 and 2) and each *outputs* a respective signal stream responsive to said detected optical radiation (Figs. 2 and 3).

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In regard to claim 2, Clarke discloses the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; Fig. 2; Col 3 lines 28-40; and Col 4 line 35 – Col 5 line 5).

In regard to claim 3, Clarke discloses the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40).

In regard to claim 4, Clarke discloses the optical source is configured to emit optical radiation at three wavelengths about 30 nm apart (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; and closely spaced wavelengths will be less than about 30nm wide, abstract and Col 3 lines 9-12).

In regard to claim 5, Clarke discloses the optical source is configured to emit optical radiation at about 1610 nm, about 1645 nm, and about 1665 nm (broadband near IR emitter, Col 5 lines 1-5 and Col 3 lines 28-40; 1600nm +/- 15nm, abstract; and about 60nm or 30nm wide, Col 3 lines 9-12).

In regard to claim 6, Clarke discloses a patient monitor capable of processing the plurality of output signal streams to determine output values for one or more physiological parameters (element 16, Figs 1 and 2).

In regard to claim 7, Clarke discloses one of the one or more physiological parameters comprises glucose (Col 3 lines 28-40).

In regard to claim 29, Clarke discloses a method of measuring an analyte based on multiple streams of optical radiation measured from a measurement site (Figs. 1-2),



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said method comprising: emitting a sequence of optical radiation pulses to the measurement site (Col 1 line 56 – Col 2 line 49; Col 4 line 5; elements 12, Fig. 2); detecting at a first location a first stream of optical radiation from the measurement site (Fig. 2 and Col 5 line 49 – Col 6 line 9); detecting at least at one additional location different from the first location an additional stream of optical radiation from the measurement site (Fig. 2 and Col 5 line 49 – Col 6 line 9); and determining an output measurement value indicative of the analyte based on the detected streams of optical radiation (Fig. 1; Col 5 lines 6-17; and Col 6 lines 1-9).

In regard to claim 30, Clarke discloses said analyte comprises glucose (Col 6 lines 1-9).

In regard to claim 30, Clarke discloses converting the detected streams of optical radiation into a digital signal including a respective stream for each location (Col 5 line 49 – Col 6 line 9).

4. Claims 8-9, 11-13, 15, 19-24, and 28-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Simonsen et al. (USPN 5,676,143). In regard to claim 8, Simonsen discloses a noninvasive, physiological sensor capable of outputting a signal responsive to a blood analyte present in a monitored patient (Figs. 13-15 and 17-18), said sensor comprising: a sensor housing (Figs. 13 and 17); an optical source (elements 27, 29 and 35, Fig. 13; elements 27 and 59, Fig. 17) positioned by said housing with respect to a tissue site of a patient (skin 33, Fig. 13; finger, Fig. 17) when said housing is applied to the patient (Figs. 13 and 17); and photodetectors (elements 36-39, Fig. 15; elements

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14k-14m of element 28, Fig. 17) positioned by said housing with respect to said tissue site when said housing is applied to the patient with a variation in path length among at least some of the photodetectors from the optical source (abstract and Figs. 15 and 17), the photodetectors configured to detect a sequence of optical radiation from said optical source after attenuation by tissue of said tissue site (abstract and Figs. 15 and 17), said photodetectors each configured to output a respective signal stream responsive to said detected sequence of optical radiation and wherein an output signal responsive to one or more of the signal streams is usable to determine the blood analyte based at least in part on the variation in path length (abstract; Col 9 lines 4-23).

In regard to claim 9, Simonsen discloses the blood analyte comprises glucose (abstract), wherein the sensor comprises electronic circuitry configured to receive said signals responsive to said detected sequence of optical radiation and wherein said output signal is indicative of said glucose (Fig. 20).

In regard to claim 11, Simonsen discloses a signal medium that is configured to connect to a processing device (Fig. 20).

In regard to claim 12, Simonsen discloses an interface configured to provide the signal to a device external to the sensor (Fig. 20).

In regard to claim 13, Simonsen discloses the interface comprises at least one transimpedance amplifier configured to amplify the signal stream from the photodetectors (Fig. 20).

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In regard to claim 15, Simonsen discloses the housing comprises a shell constructed of material capable of reflecting at least some of the optical radiation back into the tissue site (aluminum 53, Fig. 17).

In regard to claim 19, Simonsen discloses the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site (Col 18, lines 40-49).

In regard to claim 20, Simonsen discloses an optical noise reducer capable of reducing ambient light from entering the tissue site (elements 31a and 31b, Fig. 13 and col 18, lines 56-64).

In regard to claim 21, Simonsen discloses a heat sink configured to dissipate heat from the sensor (aluminum 53, Fig. 17 and Col 19, lines 30-37).

In regard to claim 22, Simonsen discloses the photodetectors are arranged in a special geometry (Figs. 7-12, 15, and 17-19).

In regard to claim 23, Simonsen discloses the special geometry comprises a substantially linear geometry (Figs. 7-12 and 15).

In regard to claim 24, Simonsen discloses the special substantially linear geometry comprises substantially equal spacing (Fig. 10).

In regard to claim 28, Simonsen discloses the special geometry comprises a substantially grid geometry (Fig. 12).

In regard to claims 29-31, claims 29-31 encompass the similar scope of the invention as that of the claims 8-9. Therefore, claims 29-31 are rejected on the same ground as the claims 8-9.

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5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen. In regard to claim 10, Simonsen discloses all the claimed limitations except a display coupled to the sensor housing and configured to display information indicating the blood analyte. Simonsen discloses a microcomputer unit (element 74, Fig. 20) configured to calculate the concentration of blood analyte (abstract). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the sensor to be coupled to a display in order to output/ show the calculation results to the user.

7. Claim 14 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen as applied to claim 8 above, and further in view of Shaw et al. (USPN 4,114,604). In regard to claim 14, Simonsen discloses all the claimed limitations except the interface comprises at least one switched capacitor circuit configured to convert said signal stream from the photodetectors into digital information. Shaw teaches at least one switched capacitor circuit configured to convert said signal stream from the photodetectors into digital information (element 17, Fig. 1 and Col 4 line 62 – Col 5 line 8). Simonsen discloses amplifiers (elements 71a-c and 72a-c) for converting the

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detected signals into digital signals. Shaw teaches using the operationally connected capacitor which compensates for amplifier drift and spurious outputs from the detector (Col 5 lines 1-8). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the interface (Simonsen) to incorporate the switched capacitor circuit (Shaw) in order to obtain more accurate optical measurements.

In regard to claims 25-27, Simonsen discloses all the claimed limitations except the special substantially linear geometry comprises substantially unequal spacing which comprises substantially logarithmic spacing/ progressive spacing. However, Simonsen discloses various detector arrangements (Figs. 7-12 and 15) comprising an unequal spacing configuration (Fig. 11). It is known that the Beer-Lambert law contains exponential relationships of light absorption/ attenuation and the spacing between detectors associated to the light emitter is proportional to the light propagating length. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the spacing between detectors with logarithmic spacing/ progressive spacing through experiments or mathematical relationships to yield predictable results.

8. Claims 16-18 and 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonsen as applied to claims 8 and 29 above, and further in view of Toida (USPGPUB 2002/0052547). In regard to claims 16-18 and 32-34, Simonsen discloses the optical source comprises at least one set of sources comprising at least

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one light emitting diode and other semi-conductor light sources (Col 5 lines 6-37) and the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm (Col 5 lines 6-37). However, Simonsen does not specifically disclose at least one super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm. Toida teaches a super-luminescent light emitting diode configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm ([0007] and [0025]). Simonsen discloses the light emitting diode or other semi-conductor light sources emitting discrete wavelengths can be used in order to reduce the cost of the apparatus. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute one of the light emitting diode or one of other semi-conductor light sources emitting light in approximately 1650 to approximately 1800 nm (Simonsen) with the SLD (Toida) to yield predictable results.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHU CHUAN (JJ) LIU whose telephone number is (571)270-5507. The examiner can normally be reached on M-TH 8:00am~4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tse Chen can be reached on (571)272-3672. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chu Chuan Liu/  
Examiner, Art Unit 3777

/Eric F Winakur/  
Primary Examiner, Art Unit 3777

<b>Notice of References Cited</b>	Application/Control No. 12/534,827	Applicant(s)/Patent Under Reexamination POEZE ET AL.	
	Examiner CHU CHUAN (JJ) LIU	Art Unit 3777	Page 1 of 1

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*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-4,114,604	09-1978	Shaw et al.	356/41
*	B	US-5,222,496	06-1993	Clarke et al.	600/316
*	C	US-5,676,143	10-1997	Simonsen et al.	600/316
*	D	US-2002/0052547	05-2002	Toida, Masahiro	600/425
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

**FOREIGN PATENT DOCUMENTS**


*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

**NON-PATENT DOCUMENTS**

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	


\*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)  
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.



<b><i>Index of Claims</i></b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

✓	<b>Rejected</b>	-	<b>Cancelled</b>	N	<b>Non-Elected</b>	A	<b>Appeal</b>
=	<b>Allowed</b>	÷	<b>Restricted</b>	I	<b>Interference</b>	O	<b>Objected</b>

<input type="checkbox"/> Claims renumbered in the same order as presented by applicant											<input type="checkbox"/> CPA		<input type="checkbox"/> T.D.		<input type="checkbox"/> R.1.47	
CLAIM		DATE														
Final	Original	09/17/2012														
	1	✓														
	2	✓														
	3	✓														
	4	✓														
	5	✓														
	6	✓														
	7	✓														
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	32	✓														
	33	✓														
	34	✓														

<b>Search Notes</b> 	<b>Application/Control No.</b> 12534827	<b>Applicant(s)/Patent Under Reexamination</b> POEZE ET AL.
	<b>Examiner</b> CHU CHUAN (JJ) LIU	<b>Art Unit</b> 3777

SEARCHED			
Class	Subclass	Date	Examiner
600	310, 316, 322, 323, 326, 340, 344, 473, 476	09/17/2012	CCL
356	41	09/17/2012	CCL

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor Name Search (PALM, EAST)	09/10/2012	CCL
East Search (TEXT, USPGPUB, USPAT) See Search History	09/17/2012	CCL
Google NPL Search	09/17/2012	CCL

INTERFERENCE SEARCH			
Class	Subclass	Date	Examiner

/CHU CHUAN (JJ) LIU/  
Examiner.Art Unit 3777

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534,827
	Filing Date	August 3, 2009
	First Named Inventor	Jeroen Poeze
	Art Unit	3768
	Examiner	Winakur, Eric Frank
SHEET 1 OF 1	Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	2004/049237	03-11-2004	Larson, et al.	
	2	4,258,719	03-31-1981	Lewyn	
	3	5,676,143	10-14-1997	Simonsen, et al.	
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Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>
	6	WO 2000/25112	05-04-2000	Rolfe		

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	7	International Search Report issued in Application No. PCT/US2009/052756, mailed February 10, 2009 in 14 pages.	
	8	International Preliminary Report on Patentability and Written Opinion of the International Searching Authority issued in Application No. PCT/US2009/052756, mailed February 8, 2011 in 8 pages.	

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Examiner Signature	/Chu Chuan Liu/	Date Considered	09/17/2012
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

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PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827	
	Filing Date	08-03-2009	
	First Named Inventor	Poeze, Jeroen et al	
	Art Unit	3768	
SHEET 1 OF 9		Examiner	Unknown
		Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
SHEET 2 OF 9		Attorney Docket No. MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
	Examiner	Unknown
SHEET 3 OF 9	Attorney Docket No.	MLHUM.002A

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Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
(Multiple sheets used when necessary)	Examiner	Unknown
SHEET 4 OF 9	Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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Examiner Signature	Date Considered
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PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
(Multiple sheets used when necessary)	Examiner	Unknown
SHEET 5 OF 9	Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	117	6,721,582	04/2004	Trepagnier, et al.	
	118	RE38,492	04/2004	Diab et al.	
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Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827	
	Filing Date	08-03-2009	
	First Named Inventor	Poeze, Jeroen et al	
	Art Unit	3768	
(Multiple sheets used when necessary)		Examiner	Unknown
SHEET 6 OF 9		Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	146	6,525,386	02/2003	Mills et al.	
	147	6,519,487	02/2003	Parker	
	148	6,515,273	02/2003	Al-Ali	
	149	6,505,059	01/2003	Kollias, et al.	
	150	6,501,975	12/2002	Diab et al.	
	151	6,470,199	10/2002	Kopotic et al.	
	152	6,463,311	10/2002	Diab	
	153	6,430,525	08/2002	Weber et al.	
	154	6,397,091	05/2002	Diab et al.	
	155	6,388,240	05/2002	Schulz et al.	
	156	6,377,829	04/2002	Al-Ali	
	157	6,371,921	04/2002	Caro et al.	
	158	6,368,283	04/2002	Xu, et al.	
	159	6,360,114	03/2002	Diab et al.	
	160	6,349,228	02/2002	Kiani et al.	
	161	6,343,224	01/2002	Parker	
	162	6,334,065	12/2001	Al-Ali et al.	
	163	6,321,100	11/2001	Parker	
	164	6,285,896	09/2001	Tobler et al.	
	165	6,280,213	08/2001	Tobler et al.	
	166	6,278,522	08/2001	Lepper, Jr. et al.	
	167	6,263,222	07/2001	Diab et al.	
	168	6,256,523	07/2001	Diab et al.	
	169	6,241,683	06/2001	Macklem, et al.	
	170	6,236,872	05/2001	Diab et al.	
	171	6,232,609	05/2001	Snyder, et al.	
	172	6,229,856	05/2001	Diab et al.	
	173	6,206,830	03/2001	Diab et al.	
	174	6,184,521	02/2001	Coffin, IV et al.	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
	Examiner	Unknown
SHEET 7 OF 9	Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	175	6,165,005	12/2000	Mills et al.	
	176	6,157,850	12/2000	Diab et al.	
	177	6,152,754	11/2000	Gerhardt et al.	
	178	6,151,516	11/2000	Kiani-Azarbayjany et al.	
	179	6,144,868	11/2000	Parker	
	180	6,124,597	09/2000	Shehada	
	181	6,110,522	08/2000	Lepper, Jr. et al.	
	182	6,088,607	07/2000	Diab et al.	
	183	6,081,735	06/2000	Diab et al.	
	184	6,067,462	05/2000	Diab et al.	
	185	6,045,509	04/2000	Caro et al.	
	186	6,036,642	03/2000	Diab et al.	
	187	6,027,452	02/2000	Flaherty et al.	
	188	6,011,986	01/2000	Diab et al.	
	189	6,002,952	12/1999	Diab et al.	
	190	5,997,343	12/1999	Mills et al.	
	191	5,995,855	11/1999	Kiani et al.	
	192	5,940,182	08/1999	Lepper, Jr. et al.	
	193	5,934,925	08/1999	Tobler et al.	
	194	5,919,134	07/1999	Diab	
	195	5,904,654	05/1999	Wohltmann et al.	
	196	5,890,929	04/1999	Mills et al.	
	197	5,860,919	01/1999	Kiani-Azarbayjany et al.	
	198	5,833,618	11/1998	Caro et al.	
	199	5,830,131	11/1998	Caro et al.	
	200	5,823,950	10/1998	Diab et al.	
	201	5,810,734	09/1998	Caro et al.	
	202	5,791,347	08/1998	Flaherty et al.	
	203	5,785,659	07/1998	Caro et al.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
	Examiner	Unknown
SHEET 8 OF 9	Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	204	5,782,757	07/1998	Diab et al.	
	205	5,769,785	06/1998	Diab et al.	
	206	5,760,910	06/1998	Lepper, Jr. et al.	
	207	5,758,644	06/1998	Diab et al.	
	208	5,743,262	04/1998	Lepper, Jr. et al.	
	209	Des. 393,830	04/1998	Tobler et al.	
	210	5,685,299	11/1997	Diab et al.	
	211	5,645,440	07/1997	Tobler et al.	
	212	5,638,818	06/1997	Diab et al.	
	213	5,638,816	06/1997	Kiani-Azarbayjany et al.	
	214	5,632,272	05/1997	Diab et al.	
	215	5,602,924	02/1997	Durand et al.	
	216	5,590,649	01/1997	Caro et al.	
	217	5,562,002	10/1986	Lalin	
	218	5,561,275	10/1996	Savage, et al.	
	219	5,533,511	07/1996	Kaspari et al.	
	220	5,494,043	02/1996	O'Sullivan et al.	
	221	5,490,505	02/1996	Diab et al.	
	222	5,482,036	01/1996	Diab et al.	
	223	D363,120	10/1995	Savage et al.	
	224	5,456,252	10/1995	Vari, et al.	
	225	5,452,717	09/1995	Branigan et al.	
	226	D362,063	09/1995	Savage et al.	
	227	D361,840	08/1995	Savage et al.	
	228	D359,546	06/1995	Savage, et al.	
	229	5,431,170	07/1995	Mathews	
	230	D353,196	12/1994	Savage et al.	
	231	D353,195	12/1994	Savage et al.	
	232	5,278,627	01/1994	Aoyagi et al.	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827	
	Filing Date	08-03-2009	
	First Named Inventor	Poeze, Jeroen et al	
	Art Unit	3768	
(Multiple sheets used when necessary)		Examiner	Unknown
SHEET 9 OF 9		Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	233	5,377,676	01/1995	Vari, et al.	
	234	5,341,805	08/1994	Stavridi, et al.	
	235	5,337,744	08/1994	Branigan	
	236	5,163,438	11/1992	Gordon et al.	
	237	5,069,213	12/1991	Polczynski	
	238	5,041,187	08/1991	Hink et al.	
	239	4,964,408	10/1990	Hink et al.	
	240	4,960,128	10/1990	Gordon et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>
	241	WO93/12712	07-08-1993	Vivascan Corp		

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	242	International Search Report and Written Opinion for PCT/US2009/049638, mailed January 7, 2010.	

Examiner Signature	/Chu Chuan Liu/	Date Considered	09/17/2012
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>			

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CX-1621

PTO/SB/08 Equivalent

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Multiple sheets used when necessary)

SHEET 1 OF 1

Application No.	12/534,827
Filing Date	August 3, 2009
First Named Inventor	Poeze, et al.
Art Unit	3768
Examiner	Unknown
Attorney Docket No.	MLHUM.002A

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	4,267,844	05/19/1981	Yamanishi	
	2	4,655,225	04/07/1987	Dähne, et al.	
	3	4,781,195	11/01/1988	Martin	
	4	4,805,623	02/21/2989	Jöbsis	
	5	5,028,787	07/02/1991	Rosenthal, et al.	
	6	5,077,476	12/31/1991	Rosenthal	
	7	5,137,023	08/11/1992	Mendelson, et al.	
	8	5,337,745	08/16/1994	Benaron	

## FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>
	9	EP419223	03/27/1991	Minnesota Mining and Manufacturing Company		

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	10	Burritt, Mary F.; Current Analytical Approaches to Measuring Blood Analytes; Vol. 36; No. 8(B); 1990	
	11	Hall, et al., Jeffrey W.; Near-Infrared Spectrophotometry: A New Dimension in Clinical Chemistry; Vol. 38; No. 9; 1992	
	12	Kuenstner, et al., J. Todd; Measurement of Hemoglobin in Unlysed Blood by Near-Infrared Spectroscopy; Vol. 48; Number 4, 1994	
	13	Manzke, et al., B., Multi Wavelength Pulse Oximetry in the Measurement of Hemoglobin Fractions; Vol. 2676	
	14	Naumenko, E. K.; Choice of Wavelengths for Stable Determination of Concentrations of Hemoglobin Derivatives from Absorption Spectra of Erythrocytes; Vol. 63; No. 1; pp. 60-66 January - February 1996; Original article submitted November 3, 1994	
	15	Schmitt, Joseph M.; Simple Photon Diffusion Analysis of the Effects of Multiple Scattering on Pulse Oximetry; March 14, 1991; revised August 30, 1991	
	16	Schmitt, et al., Joseph M.; Measurement of Blood Hematocrit by Dual-Wavelength near-IR Photoplethysmography; Vol. 1641; 1992	
	17	Schnapp, et al., L.M.; Pulse Oximetry. Uses and Abuses.; Chest 1990; 98; 1244-1250 DOI 10.1378/Chest.98.5.1244	

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Examiner Signature	/Chu Chuan Liu/	Date Considered	09/17/2012
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\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

Appx57928

**EAST Search History****EAST Search History (Prior Art)**

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L3	161	(super adj luminescent with diode SLD) and nm and "600".clas.	US-PGPUB; USPAT	OR	ON	2012/09/17 07:28
L7	0	unequal adj spacing same detector and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/17 07:44
L8	11	unequal adj spacing and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/17 07:44
L9	671	spacing and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/17 07:45
L10	226	spacing with detector and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/17 07:45
L11	48	sensor with unequal with spacing	US-PGPUB; USPAT	OR	ON	2012/09/17 07:58
L12	5	sensor with progressive with spacing	US-PGPUB; USPAT	OR	ON	2012/09/17 08:00
L13	13	sensor with (log logarithm) with spacing	US-PGPUB; USPAT	OR	ON	2012/09/17 08:05
L14	1089	(log logarithm) with spacing	US-PGPUB; USPAT	OR	ON	2012/09/17 08:07
L15	69	(log logarithm) with spacing with linear	US-PGPUB; USPAT	OR	ON	2012/09/17 08:07
L16	238	(log logarithm\$2) with spacing with linear	US-PGPUB; USPAT	OR	ON	2012/09/17 08:07
L17	182	( logarithm\$2) with spacing with linear	US-PGPUB; USPAT	OR	ON	2012/09/17 08:09
L18	59	non\$linear with spacing and "600".clas.	US-PGPUB; USPAT	OR	ON	2012/09/17 08:27
L19	10	exponential with spacing and "600".clas.	US-PGPUB; USPAT	OR	ON	2012/09/17 08:38
S1	1	(12/534827).APP.	US-PGPUB; USPAT	OR	OFF	2012/09/10 06:54
S2	208	(Poeze near2 Jeroen Lamego near2 Marcelo Merritt near2 Sean Dalvi near2 Cristiano Vo	US-PGPUB;	OR	ON	2012/09/10 06:55

EAST Search History

CX-1621

		near2 Hung Bruinsma near2 Johannes Lesmana near2 Ferdyan Kiani near3 Massi).in.	USPAT			
S3	71	S2 and glucose	US-PGPUB; USPAT	OR	ON	2012/09/10 07:28
S4	40	S2 and glucose and nm	US-PGPUB; USPAT	OR	ON	2012/09/10 07:28
S5	253	( "20060211924"   "5482036"   "5997343"   "6002952"   "6027452"   "6165005"   "6263222"   "6321100"   "6345194"   "6397091"   "6542764"   "6699194"   "6714804"   "6745060"   "6816741"   "6931268"   "7027849"   "7132641"   "7225006"   "7272425"   "7274955"   "7280858"   "7377794"   "7415297"   "7454240"   "7469157"   "7483729"   "7489958"   "7496391"   "7499835"   "D554263"   "4258719"   "5676143"   "6816241"   "5069213"   "5452717"   "5456252"   "5561275"   "5638816"   "5833618"   "6152754"   "6232609"   "6241683"   "6606511"   "6640116"   "6661161"   "6721585"   "6792300"   "6861639"   "7039449"   "7096052"   "7186966"   "7225007"   "7239905"   "7332784"   "7340287"   "7343186"   "7496393"   "7596398"   "D353195"   "RE38476"   "4805623"   "5137023"   "6172743"   "20040054291"   "4960128"   "5163438"   "5758644"   "5769785"   "5782757"   "5810734"   "5904654"   "5940182"   "6206830"   "6280213"   "6334065"   "6349228"   "6368283"   "6515273"   "6541756"   "6597932"   "6697657"   "6728560"   "6950687"   "7030749"   "7067893"   "7254953"   "7289835"   "7328053"   "7438683"   "7526328"   "D361840"   "D362063"   "D587657"   "5028787"   "5377676"   "5602924"   "5645440"   "5791347"   "5890929"   "5919134"   "6045509"   "6110522"   "6184521"   "6236872"   "6278522"   "6377829"   "6463311"   "6584336"   "6597933"   "6658276"   "6760607"   "6770028"   "6943348"   "6970792"   "6985764"   "6993371"   "7003338"   "7149561"   "7215984"   "7292883"   "7341559"   "7563110"   "7618375"   "4781195"   "20040049237"   "5341805"   "5685299"   "5785659"   "6088607"   "6124597"   "6151516"   "6157850"   "6360115"   "6526300"   "6650917"   "6654624"   "6771994"   "6830711"   "6850787"   "6934570"   "7015451"   "7044918"   "7254433"   "7254434"   "7355512"   "7371981"   "7373193"   "7471971"   "7530942"   "7530949"   "D606659"   "4267844"   "4655225"   "4964408"   "5278627"   "5562002"   "5590649"   "5743262"   "5823950"   "5934925"   "6011986"   "6067462"   "6285896"   "6343224"	US-PGPUB; USPAT	OR	ON	2012/09/10 07:50

EAST Search History

CX-1621

		"6360114"   "6371921"   "6388240"   "6643530"   "6697656"   "6697658"   "6822564"   "6826419"   "6852083"   "6920345"   "6999904"   "7190261"   "7295866"   "7373194"   "7377899"   "7509494"   "7647083"   "D359546"   "D363120"   "RE38492"   "RE39672"   "20090259114"   "5760910"   "5860919"   "6036642"   "6081735"   "6229856"   "6430525"   "6501975"   "6505059"   "6525386"   "6639668"   "6678543"   "6684090"   "6684091"   "6721582"   "6725075"   "6813511"   "6850788"   "6898452"   "7024233"   "7096054"   "7376453"   "7383070"   "7428432"   "7499741"   "7509154"   "5077476"   "5041187"   "5337744"   "5431170"   "5490505"   "5494043"   "5533511"   "5632272"   "5638818"   "5830131"   "5995855"   "6144868"   "6256523"   "6470199"   "6519487"   "6580086"   "6595316"   "6632181"   "6671531"   "6735459"   "6939305"   "6961598"   "6979812"   "6996427"   "7003339"   "7041060"   "7142901"   "7215986"   "7221971"   "7254431"   "7440787"   "7467002"   "7471969"   "7483730"   "7500950"   "7530955"   "D353196"   "D393830"   "D566282"   "D609193"   "5337745").PN.				
S6	70	S5 and glucose and nm	US-PGPUB; USPAT	OR	ON	2012/09/10 07:50
S7	0	S6 and ("16"?2 "17"?2) adj nm	US-PGPUB; USPAT	OR	ON	2012/09/10 07:51
S8	7	S6 and ("1600" "1700") adj nm	US-PGPUB; USPAT	OR	ON	2012/09/10 07:52
S9	123	NIR and glucose and 600/310-344.ccls. and broadband	US-PGPUB; USPAT	OR	ON	2012/09/10 09:48
S10	161	capacitor with switch\$3 and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:21
S11	161	switch\$3 with capacitor and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:23
S12	20	super adj luminescent with light adj emitting adj diode and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:39
S13	55	(super adj luminescent with light adj emitting adj diode SLD) and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:40
S14	13	(super adj luminescent with light adj emitting adj diode SLD) and nir and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:46
S15	11	(super adj luminescent with light adj emitting adj diode SLD) and ("1600" "1700" "1800" "2500") with nm and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:49



EAST Search History

CX-1621

S16	11	(super adj luminescent with diode SLD) and ("1600" "1700" "1800" "2500") with nm and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:51
S17	35	(super adj luminescent with diode SLD) and nm and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:51
S18	22	(super with luminescent with diode SLD) and nm and glucose and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:53
S19	35	(super with luminescent with diode SLD) and nm and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:56
S20	161	(super with luminescent with diode SLD) and nm and "600".clas.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:56
S21	26	(super adj luminescent with diode SLD) and ("1600" "1700" "1800" "2500") with nm and "600".clas.	US-PGPUB; USPAT	OR	ON	2012/09/10 10:57
S22	93	heat adj sink and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 11:15
S23	47	logarithmic with (detectors array) and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 11:31
S24	52	logarithmic with (detectors array spac\$3) and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2012/09/10 11:35
S25	5	S24 not S23	US-PGPUB; USPAT	OR	ON	2012/09/10 11:35
S26	1	("6731248").PN.	US-PGPUB; USPAT	OR	OFF	2012/09/10 11:39
S27	161	log with periodic with array and detector	US-PGPUB; USPAT	OR	ON	2012/09/10 11:39

**EAST Search History (Interference)**

&lt; This search history is empty &gt;

**9/ 17/ 2012 8:44:05 AM****C:\ Users\ cliu\ Documents\ EAST\ Workspaces\ 12534827.wsp**

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534,827
	Filing Date	August 3, 2009
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**U.S. PATENT DOCUMENTS**

Examiner Initials	Cite No.	Document Number <i>Number - Kind Code (if known)</i> Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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	6	WO 2000/25112	05-04-2000	Rolfe		

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	7	International Search Report issued in Application No. PCT/US2009/052756, mailed February 10, 2009 in 14 pages.	
	8	International Preliminary Report on Patentability and Written Opinion of the International Searching Authority issued in Application No. PCT/US2009/052756, mailed February 8, 2011 in 8 pages.	

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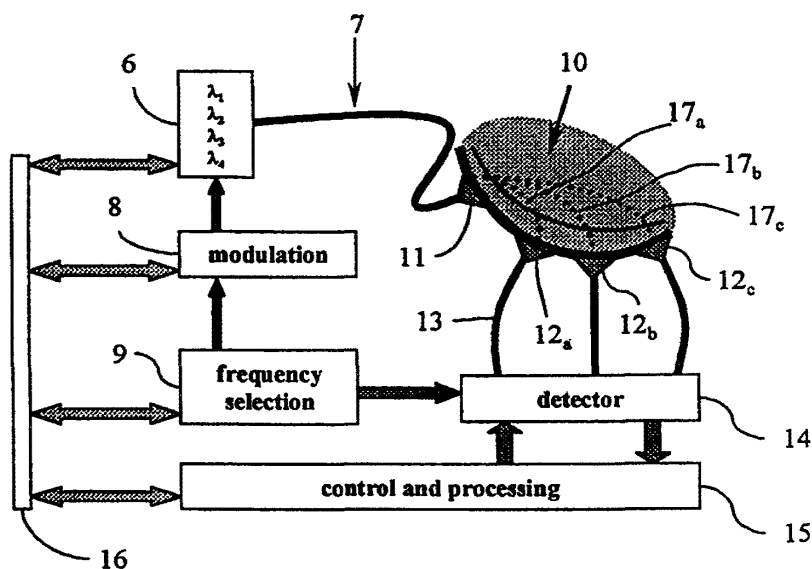
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**(54) Title:** OPTICAL MONITORING**(57) Abstract**

An optical monitoring method is disclosed by means of which the absolute concentration of chemical or biological species of interest may be determined in tissue *in vivo*. Electromagnetic radiation – typically near infrared – is directed through the tissue of interest and emergent radiation is sampled from at least three points with different direct physical path lengths. Signal processing in real time is applied to the emergent radiation. Apparatus for use in this method is also disclosed.



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### Optical Monitoring

This invention is concerned with improvements to methods used for non-invasive monitoring of patients using electromagnetic energy.

5 It is desirable to obtain indications of the concentrations of certain chemicals in various parts of the body in order to detect abnormal and dangerous conditions. Examples of chemicals of interest include those which are linked to the transport or utilisation of oxygen, such as oxy and de-oxy haemoglobin in blood, oxy and de-oxy myoglobin in muscle or oxidised and reduced intra-cellular enzymes such as cytochrome aa<sub>3</sub>. Other chemicals of interest include glucose in blood or tissue or  
10 cholesterol in blood.

The purpose of determining such chemical concentrations is to allow correction of abnormal and dangerous conditions and it is therefore desirable to carry out repeated measurements or continuous real-time measurements. This is particularly desirable when measuring those chemicals linked to transport or utilisation of  
15 oxygen because the concentrations of these are known to be liable to change very rapidly; significant changes can occur in 5-10 seconds.

In order for abnormal and dangerous conditions to be determined it is also necessary for the measurement of chemical concentration to be made in a quantitative way so that comparison with accepted normal values might be made.

20 It is known that electromagnetic energy can pass through tissue and that when wavelengths in the near infra-red region of the spectrum are used then deeper penetration of tissues is possible as compared to that achieved with visible wavelengths.

It is also known that by interrogating tissue with two or more specific wavelengths of

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electromagnetic energy, followed by mathematical analysis of the intensity of the energy emerging from passage through the tissue, it is possible to determine estimates of the changes in concentration of one or more chemical species in the tissue being interrogated. In order to perform the calculation use is made of the Beer-Lambert law. Here it is given for a single absorber and a single wavelength of measurement.

$$A_1 = \log \frac{\mathcal{I}_0}{\mathcal{I}} = e_1 C_1 d_p \zeta + \Psi \quad \text{Equation 1}$$

in which  $A_1$  is the **attenuation** of the electromagnetic wave measured in optical density units (OD),  $\mathcal{I}_0$  is the incident wave intensity,  $\mathcal{I}$  is the intensity of the wave emerging from the tissue,  $e_1$  is the **specific extinction coefficient** of the absorbing compound in  $\mu\text{molar}^{-1}.\text{cm}^{-1}$ ,  $C_1$  is the **concentration** of the absorbing compound and  $d_p$  is the **distance** in cm between the points where the wave enters and emerges from the tissue. Due to scattering of the electromagnetic wave in tissue its path will be longer than the physical spacing by a **factor**  $\zeta$ , known as the **scattering factor**. Attenuation of the wave also occurs due to scattering and an **additive term**,  $\Psi$ , is used to describe this. It is useful to consider the product  $e.C$  as the **absorption coefficient**,  $\mu_a$ .

Problems arise with this method of monitoring chemical variables in patients because it is not possible to determine absolute chemical concentration. This is partly because the scattering factor,  $\zeta$ , is not known and partly because the additive term,  $\Psi$ , is not known. Instead of calculating absolute chemical concentration, therefore, it is now common practice to measure changes in attenuation from an arbitrary starting point and from such changes in attenuation to calculate changes in chemical concentration.

Although in some circumstances this current method can provide useful information for the monitoring of patients it is a disadvantage that it is not possible to determine

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absolute quantitative values of the chemical concentrations. This means that measurements made in one subject can not be compared with those made in another subject and measurements made in one subject on one occasion can not be compared with measurements made in that subject on a second or subsequent occasion.

The absolute chemical concentrations can be determined if certain effects of scattering can be measured and if other certain effects of scattering can be modelled mathematically and if these steps can be performed rapidly and cost-effectively. This approach is the essence of the present invention.

As indicated in equation 1, one effect of scattering in tissues is that the length of the path travelled by the interrogating wave is greater than the physical distance,  $d_p$ . In fact the so-called optical pathlength,  $d_o$  is greater than  $d_p$  by something like 3 to 5 times depending on the tissue type and the wavelength of light.

This effect of scattering could be taken into account if  $d_o$  could be measured. It is known that there are at least two methods to measure optical path length.

Firstly, the time taken for a short pulse of electromagnetic energy at the appropriate wavelength to travel through the tissue can be measured and distance then calculated as:

20

$$d_o = c.t$$

Equation 2

where  $c$  is the velocity of light in the tissue and  $t$  is the time taken for passage of the short pulse through the tissue. Due to the high speed of light the value of  $t$  is very short for tissue path lengths of a few cms and so there are practical problems in its measurement. It is known that very short pulses of infra-red light, in the order of a

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few psecs, can be produced by means of lasers and it is also known that such short pulses can be detected by a streak camera and these devices may be used together to measure optical path length in human tissues. However, this apparatus is large, costly, and can not be used in routine clinical circumstances.

- 5 A second method to measure optical pathlength in tissue is based on the modulation, for example with a sinusoidal function, of the intensity of the light beam passed into the tissue. In this case the intensity of the light emerging from the tissue will also vary sinusoidally but the phase of this intensity variation will lag that of the incident beam by an amount that is proportional to the optical pathlength.
- 10 Thus measurement of the phase shift between the incident and detected beams will allow optical pathlength to be calculated.

- Complications arise in practice due to the multiplicity of scattering events in tissue. This situation leads to a multiplicity of optical paths, each producing a corresponding phase-shift. The resulting received optical intensity therefore
- 15 contains a summation of phase-shifted components representing the group of scattered paths. In order to derive a useful estimate of optical path length, for example the mean, the received wave intensity must be analysed rapidly in order that the estimate may be used to provide continuous real-time calculations of chemical concentration.

- 20 The phase-shift method can be implemented easily, and at comparatively low cost, when the object under investigation contains relatively few scattering discontinuities. Under these circumstances there is a small number of scattering paths, and the summated signal at the receiver may be analysed using high frequency phase sensitive circuits. However, tissue of interest such as the brain,
- 25 limbs, liver, kidneys, muscle, bone all scatter significantly and in thick sections there will be substantial attenuation of the incident wave as well as multiple-path mixing contained in the received signal.

According to one aspect of the present invention, there is provided a method of



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determining the concentration of a selected chemical or biological species *in vivo*, in which electromagnetic radiation is directed through the tissue and emergent radiation is analysed, the frequency of the radiation being selected so as to correspond to a known absorption frequency for the species of interest and the radiation applied to the tissue being intensity modulated in accordance with a predetermined mathematical function, characterised in that:

- (i) emergent radiation is received by detectors positioned in at least three locations, each of which has a different linear separation from the radiation input;
- (ii) emergent radiation detected by said detectors is subjected to signal processing to determine, in real time, (a) the mean optical path lengths for each detector at each input wavelength; and (b) the attenuation of the input radiation at each detector and for each input wavelength; and
- (iii) the concentration of the species of interest in the tissue is calculated using known specific extinction coefficients for the species of interest at the wavelengths used and the mean optical path length and attenuation data derived from the input and emergent radiation by the signal processing step.

With preferred embodiments of the present invention there is provided means whereby an electromagnetic wave is modulated before being passed into tissue and the corresponding signals collected at three or more points after passage into and out of tissue segments containing phase information related to group optical pathlength properties are processed quickly in real-time in order to recover optical path length estimates for use in the calculation of absolute chemical concentration. There is further provided means with which phase-shifted modulation components of light propagated through tissue are analysed quickly in real-time in order to allow the attenuation due to scattering phenomena as specified by the additive term,  $\Psi$ , in equation 1 to be derived.

Subsequent combination of the two components of the information derived by the two aspects of the invention then allows calculation of absolute concentrations of

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specific chemicals within the tissue under interrogation having value for medical diagnosis or therapy.

According to a second aspect of the present invention, there is provided pparatus for use in determining the concentration of a selected chemical or biological species *in vivo*, which comprises:

5

(a) a plurality of laser diodes;

(b) a modulation circuit arranged to modulate the outputs of said laser diodes at two or more modulation frequencies;

(c) a frequency selection circuit arranged select said modulation frequencies;

10

(d) means for inputting the modulated laser radiation into human or animal tissue which is to be examined;

(e) at least three detectors for attachment to said human or animal to receive radiation emergent from said tissue; and

15

(f) signal processing means for processing data derived from said detectors, said modulation circuit and said frequency selection circuit.

One embodiment of the present invention is now described purely for illustrative purposes with reference to the accompanying drawings, in which:

Figure 1 illustrates the passage of an optical beam through animal tissue; and

Figure 2 is a schematic illustration of apparatus in accordance with this invention.

20

Referring to the drawings, Figure 1 shows a beam of electromagnetic energy [1] that has been modulated with a specific function. It will be known to those skilled in this branch of science that such energy may be considered either as a wave or as particle-like photons. The energy passes through tissue [2] that has both scattering and absorbing properties. Specific optical absorption may take place by particular

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chemical constituents in the tissue and of interest in the care of patients is the optical absorption due to the chemicals oxy-haemoglobin and deoxy-haemoglobin and the concentration of each of these chemicals individually or as some form of scaled ratio is required. There is also interest in the specific optical absorption by the intra-cellular enzyme cytochrome oxidase which may exist in the oxidised or reduced form and is known to have particular optical absorption bands in the near infra-red part of the electromagnetic spectrum for each of these two states.

The energy emerging after propagation through the tissue [3] will have been transformed by the transfer function of the tissues, including absorption by haemoglobin in its two forms and cytochrome oxidase in its oxidised and reduced state and by scattering events. The transfer function of the tissues is given by the output/input ratio,  $\mathcal{I}/\mathcal{I}_0$ ,

Extraction and analysis of the transfer function is achieved in the present invention and this is then used in the calculation of the absorption coefficient,  $\mu_a$ , and so-called reduced scattering coefficient,  $\mu_s'$ , of the tissue.

Figure 2 provides a schematic description of an instrument constructed in accordance with the present invention. In order to calculate the absolute concentrations of haemoglobin in its two forms the electromagnetic energy transmitted into the tissue consists of time-multiplexed beams of two or more wavelengths,  $\lambda_m$ , between 700 nm and 900 nm. In this particular embodiment of the present invention this is achieved by switching laser diodes [6] on and off in sequence and combining the laser diode outputs and conveying the combined energy by means of an optical fibre bundle [7] and an attachment probe [11].

During the laser ON period the intensity of the laser-generated light is modulated by a function,  $f_m$ , by means of a modulation circuit [8]. The modulation function may be sinusoidal having a frequency of  $\nu_m$ . Two or more modulating frequencies are used,  $\nu_{m1}$ ,  $\nu_{m2}$ , etc. The actual values for the present clinical applications are in the range 50 MHz to 500 MHz and are determined by a frequency selection circuit [9].

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Electromagnetic energy propagates through the tissue of interest [10] according to the structure and composition of the tissue. The energy will pass through different regions of the tissue and examples of particular paths are shown as 17<sub>a</sub>, 17<sub>b</sub> and 17<sub>c</sub>. Having propagated into the tissue of interest the energy is collected at three or  
 5 more points by means of attachments [12<sub>a</sub>, 12<sub>b</sub>, 12<sub>c</sub>], which may be connected to the signal processing elements of the system by spatially separate optical fibres; alternatively, the individual optical fibres may be bundled together for convenience.

The spacing between the input point, [11], and the collection points, [12<sub>a</sub>, 12<sub>b</sub>, 12<sub>c</sub>], has some significance. The corresponding physical pathlengths,  $(d_p)_a$ ,  $(d_p)_b$  and  $(d_p)_c$   
 10 are chosen such that there is sufficient penetration of the deeper tissue regions by electromagnetic wave paths 17<sub>a</sub>, 17<sub>b</sub> and 17<sub>c</sub>. In human tissues this means that  $(d_p)_a$  should be greater than 2.8 cms.,  $(d_p)_b$  should be greater than  $(d_p)_a$  and  $(d_p)_c$  should be greater than  $(d_p)_b$ .

In a preferred arrangement the collected energy is transported by individual optical  
 15 fibres such as [13] to a photomultiplier where it is detected and amplified [14]. An alternative arrangement may use an array of detector sensors fixed directly to the tissue surface.

With the preferred arrangement  $n_m$ ,  $v_m$ , etc. With this arrangement the signal output of the photomultiplier consists of the low frequency spectrum of 10kHz to  
 20 15kHz rather than the comparatively high frequency modulating frequency of 50 to 500 MHz and is therefore more straightforward to process. The detected optical signal contains phase shifts related to optical pathlength and intensity information in the form of a depth of modulation related to attenuation.

Whilst the heterodyne method is the preferred approach the present invention may  
 25 also be realised using well-known homodyne detection.

Mean optical path length at each wavelength and for each detector position is calculated within a control and processing unit [15] by determining the phase shift of the modulating signal. Firstly, a single modulating frequency is used and optical path

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length and modulation depths are determined for each detector position. Then, for a single detector position path length and modulation depth are determined for each of the two or more frequencies of modulation.

5 Phase shifts due to multiple optical path lengths are determined by performing a Fast Fourier Transform (FFT) within the control and processing unit [15] on the spectrum of signals available at the output of the detector unit [14]. An important aspect of the particular embodiment of the invention which facilitates accurate phase measurement is the arrangement of the control and processing unit and the specific instrument modules (6, 8, 9 and 14) which includes the use of a data and control bus.

10 The analysis of the phase-shift information from the FFT provides statistical data relating to the scattering properties of the tissue under interrogation.

In order to calculate the concentrations of oxy-haemoglobin,  $\{\text{HbO}_2\}$ , and de-oxy haemoglobin,  $\{\text{Hb}\}$ , use is made of the known approaches to electromagnetic wave transport based on the so-called diffusion approximation. This is modelled within the instrument and the approximation allows relationships to be derived between, firstly, 15 phase shift and  $\nu_m$ ,  $\mu_s'$ ,  $\mu_m$  and  $d_p$  at each wavelength,  $\lambda_n$ , of the interrogating electromagnetic wave and, secondly, the modulation depth and  $\nu_m$ ,  $\mu_s'$ ,  $\mu_m$  and  $d_p$  at each wavelength,  $\lambda_n$ . The specific measurements made by the instrument designed according to the present invention are used with the diffusion approximation in order 20 to calculate the two unknowns,  $\mu_s'$  and  $\mu_m$  for each wavelength,  $\lambda_n$ . The wavelength dependent values of the extinction coefficients for  $\text{HbO}_2$  and  $\text{Hb}$  are known. Use of these together with the calculated values of  $\mu_s'$  and  $\mu_m$  for each wavelength,  $\lambda_n$ , then allows the absolute concentrations of  $\{\text{HbO}_2\}$  and  $\{\text{Hb}\}$  to be calculated.

For clinical convenience the measurements of  $\{\text{HbO}_2\}$  and  $\{\text{Hb}\}$  are used to derive the 25 ratio  $\{\text{HbO}_2\}/[\{\text{Hb}\}+\{\text{HbO}_2\}]$  which is then expressed as a percentage by multiplication by 100 in order to produce a measurement of absolute oxygen saturation. The instrument described here as representing one embodiment of the present invention incorporates this feature.

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The continuous real-time monitoring of oxy-haemoglobin,  $\{\text{HbO}_2\}$ , and de-oxy haemoglobin,  $\{\text{Hb}\}$ , with the present invention also allows automatic correction of abnormal and dangerous levels to be achieved. For this purpose, the output of the instrument disclosed in Fig 2 is used as an input to a process control loop, the output of which is used to adjust the concentration of oxygen in the gas supply to the patient.

### Description of Operation of the Instrument

In order to perform measurements on a subject using the instrument firstly probes 11 and  $[12_a, 12_b, 12_c]$  must be affixed with appropriate spacing between the input point and the collection points. For example, for examination of the brain  $(d_p)_a$  should typically be 3 cm. In this case  $(d_p)_b$  will then be 3.8 cm and  $(d_p)_c$  will be 4.6 cm. Attachment probes 11 and  $[12_a, 12_b, 12_c]$  should also lie in a straight line.

According to the present invention the instrument will then perform a sequence of operations in order to derive quantitative values for chemical concentrations. If we consider here the measurement of  $\text{O}_2\text{Hb}$ , HHb and oxidised cytochrome aa<sub>3</sub>, three optical wavelengths, typically 760nm, 840nm and 905nm, will be required. The currently preferred sequence of operation will be:

1. Three laser diodes [6] will be switched on and off sequentially at a repetition rate of typically 1 kHz.
2. The laser ON period is divided into two parts. During the first part of the laser ON period a modulating signal of  $\nu_{m1}$  is applied to the laser. The frequency of  $\nu_{m1}$  may be typically 100 MHz. During the second part of the laser ON period a second modulating signal,  $\nu_{m2}$ , is applied to the laser. The frequency of  $\nu_{m2}$  can be 140 MHz.

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3. Energy collected at  $[12_a, 12_b, 12_c]$  during the laser ON period is fed either to a multiplexed detector, typically a photomultiplier type R6357; or to three parallel photomultipliers; or to three silicon detectors. The photomultiplier(s) will preferably have dynode drive at a frequency offset firstly from  $\nu_{m1}$  and, secondly, from  $\nu_{m2}$  by an amount which is typically 10 kHz and will thus produce an output by the heterodyne principle. If silicon detectors are used then the outputs will be mixed with a reference signal derived from  $\nu_{m1}$  and  $\nu_{m2}$  in order to produce the desired output.
4. Steps 2 and 3 are repeated for each of the laser diodes in sequence.
5. The output values produced in step 3 are used to calculate the transfer function of the interrogated tissue at each wavelength. This then allows expressions for scattering factor,  $\zeta$  and additive term,  $\Psi$ , to be determined. Application of the Beer-Lambert law then allows  $\mu_a$  and  $\mu_s'$  to be determined..
6. Based on a second aspect of the invention the output values produced in steps 3 and 4 for each collector position are used to calculate the slope values  $S_{dc}$ ,  $S_{ac}$  and  $S_{phase}$  for the DC, AC and phase expressions derived from the Diffusion Approximation of the transport equation. (For description of the Diffusion Approximation see, for example, *A Ishimaru "Diffusion of light in turbid material", Applied Optics, vol 28: 2210-2215, 1989*; the content of this document is incorporated herein reference thereto). The instrument then calculates values for  $\mu_a$  and  $\mu_s'$  from the slope expressions.
7. The values for  $\mu_a$  and  $\mu_s'$  derived either as in 5 or in 6 then allow the concentrations of O<sub>2</sub>Hb, HHb and oxidised cytochrome aa<sub>3</sub> to be calculated.
8. Selection of different wavelengths for the interrogating energy allows determination of the concentrations of other chemical species provided their molar extinction coefficients are known and are spectrally unique.

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To achieve "proof of principle" certain practical experiments have been conducted as follows.

5 The signal processing and analysis strategies were assessed using simulated signals. Signals representing the simulated phase shift signals were generated in order to test the real-time processing arrangement for extracting the tissue transfer function based on Fast Fourier Transform (FFT). A particular interest exists in determining the absorption and reduced scattering coefficients of the tissue examined due to {HbO<sub>2</sub>} and {Hb} and also due to the oxidised component of the respiratory enzyme  
10 cytochrome aa<sub>3</sub>. Therefore, for test purposes, three operating wavelengths were required in order to derive three equations that could be solved for the three unknown quantities. These were selected to be 760 nm, 840 nm 905 nm simply for the purpose of a test.

15 Two alternative implementations of the present invention have been tested.

In the first implementation, the extraction of the **scattering factor**,  $\zeta$ , and the so-called **additive term**,  $\Psi$ , from equation 1 was used. Both of these, being related to scattering phenomena, appear as unknowns. For the purpose of this proof of principle embodied  
20 with the present invention these parameters were determined by measuring the tissue transfer function at two modulating frequencies,  $\nu_{m1}$  and  $\nu_{m2}$ . The resulting set of two simultaneous equations was then solved to yield expressions for  $\zeta$  and  $\Psi$  at each interrogating wavelength. These expressions were then used with equation 1 to determine values for the absorption coefficient,  $\mu_a$ , and the reduced scattering  
25 coefficient,  $\mu_s'$ , of the tissue at each of the three wavelengths.



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In the second implementation, the use of the spatial variation of detected energy was employed. Signals simulating the modulation depth of the interrogating beam and the resulting attenuation seen in the detected beam were also fed into a digital signal processing module (DSP). The demodulation of the intensity modulated interrogating beam was then extracted successfully by an appropriate algorithm. This yielded values for a DC component and an AC component.

The extracted values of phase-shift, DC component and AC component simulated for three wavelengths and three transmit-receive distances were then used to derive values for the absorption coefficient,  $\mu_a$ , and reduced scattering coefficient,  $\mu_s'$ , of the tissue. A Diffusion approximation for photon propagation was used and both infinite and semi-infinite boundary conditions considered in order to evaluate various configurations of input point [11] and collection points [12<sub>a</sub>, 12<sub>b</sub>, 12<sub>c</sub>].

As transmit-receive distance is varied so too do DC and AC components and phase shift. A derivation from the diffusion approximation allows these relationships to be considered to be linear with slopes  $S_{dc}$ ,  $S_{ac}$  and  $S_{phase}$ . In order to extract the two unknowns,  $\mu_a$  and  $\mu_s'$ , any combination of two equations from the three linear relationships may be solved.

20

With either of the two possible methods tested for determining  $\mu_a$  and  $\mu_s'$ , the concentrations of the absorbing species of interest, that is to {HbO<sub>2</sub>}, {Hb} and the oxidised component of the respiratory enzyme cytochrome aa<sub>3</sub>, were then calculated from these using known values of absorber specific extinction coefficients at each of the three interrogating wavelengths.

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Practical measurements have been evaluated using certain modulated light sources could be used to generate the interrogating beam. It is feasible to use light emitting diodes LEDs (e.g. Hitachi type HLP 40RG) at three wavelengths,, 905 nm, 840 nm and 760 nm modulated at, for example, 48 MHz.. For extended penetration it is possible to use laser diodes e.g. Sony SLD104AU, modulated at, for example, 100 MHz. Peltier cooling of these devices is essential to achieve adequate overall signal to noise ratio.

The off-set frequency, chosen as an example to be 10 kHz., and the test phase-shifted signal were input to the DSP module where they were sampled. A conventional FFT algorithm was used to extract the phase information and this has shown successful recovery of the simulated phase-shift. Optical pathlength, which is equivalent to the product  $d_p \zeta$ , is calculated as  $(\text{phase-shift})c/2\pi\nu_m$ . Timing of analysis was programmed to test the possible use of up to four multiplexed intensity modulated light sources, emitting interrogating energy at wavelengths  $\lambda_1$ ,  $\lambda_2$ ,  $\lambda_3$  and  $\lambda_4$  selected from devices emitting at specific wavelengths between 700 nm and 1500 nm. DSP modules are available to enable, for example, 210 kHz sampling allowing more than four wavelengths to be used for determining the concentrations of more than four optically absorbing species.

20

In order to use the well-known heterodyne detection method the instrument has been tested with photomultipliers. Type R6357 may be used. Performance when modulated at the carrier plus offset, for example 100.001000 MHz, is adequate in terms of stability and linearity. Alternatively it is possible to use semiconductor detectors, for example PIN diodes, and mix the received signal with an offset reference signal to recover the phase shift and intensity information.

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The tests were carried out with optical phantoms having appropriate optical properties, of absorption and scattering. This can be produced from mixtures of milk and India ink.

5 Although the invention has been described with reference to laser sources, in particular laser diodes, it will be appreciated that the invention will operate with and includes within its scope other sources of electromagnetic radiation; one non-limiting example of such other sources is light-emitting diodes.

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## CLAIMS:

1. A method of determining the concentration of a selected chemical or biological species *in vivo*, in which electromagnetic radiation is directed through the tissue and emergent radiation is analysed, the wavelength of the radiation being selected so as to correspond to a known absorption frequency for the species of interest and the radiation applied to the tissue being intensity modulated in accordance with a predetermined mathematical function, characterised in that:
- (i) emergent radiation is received by detectors positioned in at least three locations, each of which has a different linear separation from the radiation input;
- (ii) emergent radiation detected by said detectors is subjected to signal processing to determine, in real time, (a) the mean optical path lengths for each detector at each input wavelength; and (b) the attenuation of the input radiation at each detector and for each input wavelength; and
- (iii) the concentration of the species of interest in the tissue is calculated using known specific extinction coefficients for the species of interest at the wavelengths used and the mean optical path length and attenuation data derived from the input and emergent radiation by the signal processing step.
2. A method according to claim 1, characterised in that the mean optical path lengths for each detector at each input wavelength are obtained by determining the phase shifts between input and emergent radiation.
3. A method according to claim 2, characterised in that the phase shifts between input and emergent radiation for each detector and at each wavelength used are determined

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by a Fast Fourier Transform algorithm.

4. A method according to claim 1, 2 or 3, characterised in that the radiation input is at one or more wavelengths in the range from 700 and 1500 nm.

5

5. A method according to claim 4, characterised in that the radiation input is at one or more wavelengths in the range from 700 to 900 nm.

10

6. A method according to any preceding claim, characterised in that the radiation input consists of a time-multiplexed beam of two or more wavelengths.

7. A method according to claim 6, characterised in that said multiplexed beam is obtained by a time-sequenced switching (on and off) of a plurality of laser diodes the outputs of which are combined to form the multiplexed beam.

15

8. A method according to any preceding claim, characterised in that the input radiation is laser-generated light and in that its intensity is modulated by a function,  $f_m$ , by means of a modulating circuit.

20

9. A method according to claim 8, characterised in that two or more modulating frequencies are used.

10. A method according to claim 9, characterised in that said modulating frequencies

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are in the range 50 MHz to 500 MHz.

11. A method according to any preceding claim, characterised in that emergent radiation is collected and is transported by individual optical fibres to a photomultiplier where it is detected and amplified.

5

12. A method according to claim 11, characterised in that the photomultiplier is used in the heterodyne mode.

13. A method according to claim 12, characterised in that one dynode is fed with a signal shifted by 10kHz to 15kHz from the modulating frequency applied to the input radiation.

10

14. A method according to any preceding claim, characterised in that (i) the species of interest are {Hb}, {HbO<sub>2</sub>} and the oxidised component of the respiratory enzyme cytochrome aa<sub>3</sub>; and (ii) the wavelengths of the input radiation are 760 nm, 840 nm and 905 nm.

15

15. Apparatus for use in determining the concentration of a selected chemical or biological species *in vivo*, which comprises:

20

(a) a plurality of electromagnetic radiation sources;

(b) a modulation circuit arranged to modulate the outputs of said radiation sources at two or more modulation frequencies;

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(c) a frequency selection circuit arranged select said modulation frequencies;

(d) means for inputting the modulated electromagnetic radiation into human or animal tissue which is to be examined;

5 (e) at least three detectors for attachment to said human or animal to receive radiation emergent from said tissue; and

(f) signal processing means for processing data derived from said detectors, said modulation circuit and said frequency selection circuit.

10 16. Apparatus as claimed in claim 15, characterised in that said electromagnetic radiation sources are laser diodes.

17. Apparatus as claimed in claim 15, characterised in that said electromagnetic radiation sources are light-emitting diodes.

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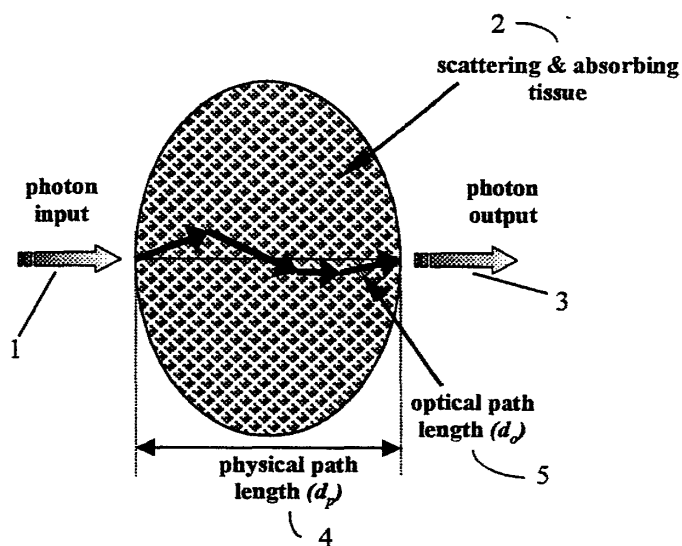


Fig 1

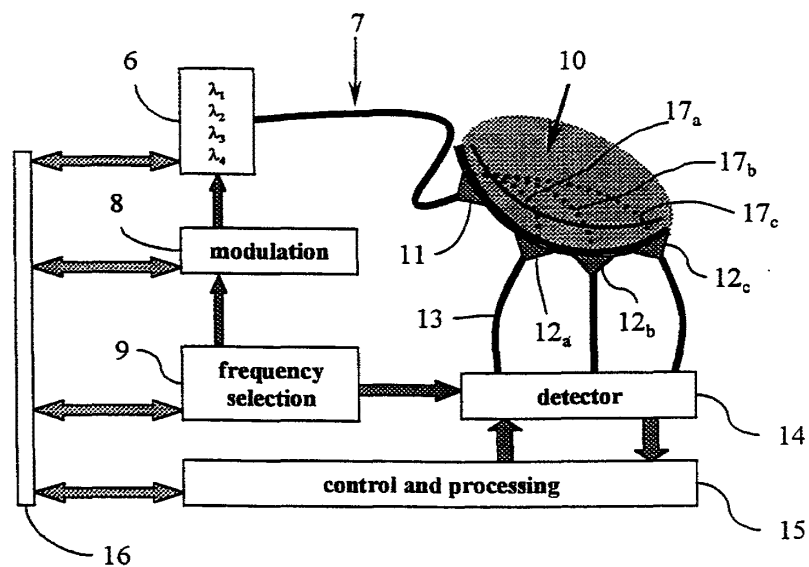


Fig 2

P Rolfe Optical  
Monitoring



## INTERNATIONAL SEARCH REPORT

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 G01N21/49		International Application No PCT/GB 99/03563
According to International Patent Classification (IPC) or to both national classification and IPC -		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 G01N		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 710 832 A (HAMAMATSU) 8 May 1996 (1996-05-08) abstract page 7, line 25 - line 35 page 9, last paragraph page 10, line 7 - line 27 page 10, line 40 - line 48 page 11, line 5 - line 17 page 11, line 22 - line 28 page 15, line 13 - line 17 claim 9; figure 7	1,4-6,8, 9,11
A	--- -/--	15,17
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.		
<input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family		
Date of the actual completion of the international search 16 February 2000		Date of mailing of the international search report 23/02/2000
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016		Authorized officer Thomas, R.M.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 99/03563

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 803 909 A (MAKI) 8 September 1998 (1998-09-08) column 1, paragraph 1 - paragraph 2 column 8, line 1 - line 30 column 10, line 43 - column 11, line 51	15-17
A	column 19, line 33 - line 58 column 20, line 26 - line 30 column 22, line 6 - line 11 column 22, line 21 - line 28 column 22, line 34 - line 46	14
Y	figures 2, 18, 20	1-9, 11
Y	US 5 752 519 A (BENARON) 19 May 1998 (1998-05-19) column 9, line 48 - column 10, line 54 column 17, line 1 - line 5 column 17, line 12 - line 19 figures 6, 7	1-9, 11
A	US 5 692 504 A (ESSENPREIS) 2 December 1997 (1997-12-02) column 10, line 26 - column 11, line 14 column 15, line 8 - line 9 column 16, line 21 - line 34 column 16, last paragraph figure 11	1, 8-12

## INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. .onal Application No

PCT/GB 99/03563

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0710832 A	08-05-1996	JP 8136448 A	31-05-1996
		US 5676142 A	14-10-1997
US 5803909 A	08-09-1998	JP 8103434 A	23-04-1996
		JP 8215179 A	27-08-1996
		JP 9019408 A	21-01-1997
US 5752519 A	19-05-1998	US 5746210 A	05-05-1998
		US 5769791 A	23-06-1998
		US 5785658 A	28-07-1998
		US 5762609 A	09-06-1998
		US 5807261 A	15-09-1998
		US 5987346 A	16-11-1999
US 5692504 A	02-12-1997	DE 4337570 A	11-05-1995
		AT 151616 T	15-05-1997
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		DE 59402462 D	22-05-1997
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		EP 0726729 A	21-08-1996
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		FI 961724 A	19-04-1996
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		IL 111525 A	24-09-1998
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		NO 961810 A	03-05-1996
		NZ 275078 A	29-01-1997
		ZA 9408666 A	03-05-1996
		AT 186395 T	15-11-1999
		AU 2342595 A	18-12-1995
		WO 9532416 A	30-11-1995
		DE 19580537 D	01-04-1999
		DE 59507189 D	09-12-1999
		EP 0760091 A	05-03-1997
		JP 10500338 T	13-01-1998

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

**PCT**

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

To:

KNOBBE, MARTENS, OLSON  
Attn: Altman, Daniel E.  
AND BEAR, LLP  
2040 Main Street, Fourteenth Floor  
Irvine, CA 92614  
ETATS-UNIS D'AMERIQUE

(PCT Rule 44.1)

Date of mailing  
(day/month/year)

02/10/2009

Applicant's or agent's file reference

MLHUM.002VPC

**FOR FURTHER ACTION**

See paragraphs 1 and 4 below

International application No.

PCT/US2009/052756

International filing date  
(day/month/year)

04/08/2009

Applicant

MASIMO LABORATORIES, INC.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70

**For more detailed instructions,** see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

**4. Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Louis Kainde

**NOTES TO FORM PCT/ISA/220**

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

**INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19**

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Volume I/A, Annexes B1 and B2).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, Volume I/A, paragraph 296).

**What parts of the international application may be amended?**

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

**When?**

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

**Where not to file the amendments?**

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

**How?**

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

**What documents must/may accompany the amendments?**

**Letter (Section 205(b)):**

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

**NOTES TO FORM PCT/ISA/220 (continued)**

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

**The following examples illustrate the manner in which amendments must be explained in the accompanying letter:**

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

**"Statement under article 19(1)" (Rule 46.4)**

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

**Consequence if a demand for international preliminary examination has already been filed**

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

If a demand for international preliminary examination is made, the written opinion of the International Searching Authority will, except in certain cases where the International Preliminary Examining Authority did not act as International Searching Authority and where it has notified the International Bureau under Rule 66.1b(b), be considered to be a written opinion of the International Preliminary Examining Authority. If a demand is made, the applicant may submit to the International Preliminary Examining Authority a reply to the written opinion together, where appropriate, with amendments before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later (Rule 43b.1(c)).

**Consequence with regard to translation of the international application for entry into the national phase**

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see the *PCT Applicant's Guide*, Volume II.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>MLHUM.002VPC</b>	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. <b>PCT/US2009/052756</b>	International filing date (day/month/year) <b>04/08/2009</b>	(Earliest) Priority Date (day/month/year) <b>04/08/2008</b>
Applicant <b>MASIMO LABORATORIES, INC.</b>		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (see Box No. III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant  
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant  
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 2b  
☒ as suggested by the applicant  
☐ as selected by this Authority, because the applicant failed to suggest a figure  
☐ as selected by this Authority, because this figure better characterizes the invention  
b. ☐ none of the figures is to be published with the abstract

Form PCT/ISA/210 (first sheet) (April 2007)

CX-1621

## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2009/052756

A. CLASSIFICATION OF SUBJECT MATTER  
INV. A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/25112 A (ROLFE PETER [GB]) 4 May 2000 (2000-05-04) abstract page 7, line 16 - page 8, line 17 page 13, lines 1-4	1-3
X	US 6 816 241 B2 (GRUBISIC DRAGAN [US]) GRUBISIC DRAGAN [US] ET AL) 9 November 2004 (2004-11-09) abstract column 1, lines 10-15, 32-38 column 3, line 66 - column 4, line 34 column 5, line 2 - column 6, line 9 column 7, lines 48-65 column 8, line 60 - column 10, line 7	1-6, 18-33
Y	----- -/--	8-17

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

## \* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

24 September 2009

Date of mailing of the international search report

02/10/2009

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
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Fax: (+31-70) 340-3016

Authorized officer

Ferrigno, Antonio

Form PCT/ISA/210 (second sheet) (April 2005)



CX-1621

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2009/052756

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2006/211924 A1 (DALKE DAVID [US] ET AL) 21 September 2006 (2006-09-21) cited in the application abstract paragraphs [0006] - [0009] paragraphs [0061] - [0066], [0068] paragraphs [0070], [0075] paragraphs [0091] - [0096], [0107] claims 1,15	1-3,5,7, 18,25, 34-36
Y	-----	8-14
X	US 6 172 743 B1 (KLEY VIC [US] ET AL) 9 January 2001 (2001-01-09) abstract column 7, lines 30-64 column 8, line 50 - column 9, line 7 -----	1,2,18, 25
X	US 5 676 143 A (SIMONSEN JAN HENNING [DK] ET AL) 14 October 1997 (1997-10-14) the whole document -----	1,2
Y	US 2004/049237 A1 (LARSON DENNIS E [US] ET AL) 11 March 2004 (2004-03-11) paragraph [0042] -----	15-17

3

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

CX-1621

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No

PCT/US2009/052756

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0025112	A	04-05-2000	EP 1125109 A1	22-08-2001
US 6816241	B2	09-11-2004	AU 9625901 A	08-04-2002
			WO 0226123 A1	04-04-2002
			US 2002041166 A1	11-04-2002
US 2006211924	A1	21-09-2006	EP 1860989 A1	05-12-2007
			EP 1860990 A1	05-12-2007
			EP 1860991 A1	05-12-2007
			EP 1860992 A1	05-12-2007
			EP 1863380 A2	12-12-2007
			EP 1860993 A1	05-12-2007
			EP 1860994 A1	05-12-2007
			EP 1860995 A1	05-12-2007
			EP 1860996 A1	05-12-2007
			EP 1895892 A1	12-03-2008
			EP 1860997 A1	05-12-2007
			JP 2008531211 T	14-08-2008
			JP 2008531212 T	14-08-2008
			JP 2008535540 T	04-09-2008
			JP 2008531214 T	14-08-2008
			JP 2008531215 T	14-08-2008
			JP 2008532589 T	21-08-2008
			JP 2008538186 T	16-10-2008
			JP 2008531216 T	14-08-2008
			JP 2008531217 T	14-08-2008
			JP 2008531218 T	14-08-2008
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			US 2008220633 A1	11-09-2008
			US 2006220881 A1	05-10-2006
			US 2006211922 A1	21-09-2006
			US 2006241358 A1	26-10-2006
			US 2006229509 A1	12-10-2006
			US 2006211923 A1	21-09-2006
			US 2006241363 A1	26-10-2006
			US 2006238358 A1	26-10-2006
			US 2006226992 A1	12-10-2006
			US 2006211925 A1	21-09-2006
			US 2006211932 A1	21-09-2006
			WO 2006094107 A1	08-09-2006
			WO 2006094108 A1	08-09-2006
			WO 2006094109 A1	08-09-2006
			WO 2006094155 A1	08-09-2006
			WO 2006115580 A2	02-11-2006
			WO 2006094168 A1	08-09-2006
			WO 2006094169 A1	08-09-2006
			WO 2006094170 A1	08-09-2006
			WO 2006094171 A1	08-09-2006
			WO 2006118654 A1	09-11-2006
			WO 2006094279 A1	08-09-2006
US 6172743	B1	09-01-2001	NONE	
US 5676143	A	14-10-1997	NONE	
US 2004049237	A1	11-03-2004	AU 2003249174 A1	02-02-2004
			EP 1521616 A2	13-04-2005
			JP 2005532870 T	04-11-2005

Form PCT/ISA/210 (patent family annex) (April 2005)

CX-1621

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No

PCT/US2009/052756

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004049237 A1		WO 2004007019 A2	22-01-2004

Form PCT/ISA/210 (patent family annex) (April 2005)

**PATENT COOPERATION TREATY**From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

**PCT****WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)**Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)Applicant's or agent's file reference  
see form PCT/ISA/220**FOR FURTHER ACTION**  
See paragraph 2 belowInternational application No.  
PCT/US2009/052756International filing date (day/month/year)  
04.08.2009Priority date (day/month/year)  
04.08.2008International Patent Classification (IPC) or both national classification and IPC  
INV. A61B5/00Applicant  
MASIMO LABORATORIES, INC.**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA:



European Patent Office  
P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040  
Fax: +31 70 340 - 3016

Date of completion of  
this opinionsee form  
PCT/ISA/210

Authorized Officer

Ferrigno, Antonio

Telephone No. +31 70 340-2174



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/052756

---

**Box No. I Basis of the opinion**

---

1. With regard to the **language**, this opinion has been established on the basis of:
  - ☒ the international application in the language in which it was filed
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ on paper
    - ☐ in electronic form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in electronic form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2009/052756

---

**Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or  
industrial applicability; citations and explanations supporting such statement**

---

1. Statement

Novelty (N)	Yes: Claims	<u>8-17, 19-24, 28-30</u>
	No: Claims	<u>1-7, 18, 25-27, 31-36</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-36</u>
Industrial applicability (IA)	Yes: Claims	<u>1-36</u>
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/052756

**Re Item V.**

**1 Reference is made to the following documents:**

- D1 : WO 00/25112 A (ROLFE PETER [GB]) 4 May 2000 (2000-05-04)
- D2 : US 6816241 B2 (GRUBISIC DRAGAN [US] GRUBISIC DRAGAN [US] ET AL) 09 November 2004 (2004-11-09)
- D3 : US 2006/211924 A1 (DALKE DAVID [US] ET AL) 21 September 2006 (2006-09-21) cited in the application
- D4 : US 6 172 743 B1 (KLEY VIC [US] ET AL) 9 January 2001 (2001-01-09)
- D5 : US 5 676 143 A (SIMONSEN JAN HENNING [DK] ET AL) 14 October 1997 (1997-10-14)
- D6 : US 2004/049237 A1 (LARSON DENNIS E [US] ET AL) 11 March 2004 (2004-03-11)

US 4 258 719 A (LEWYN LANNY L) 31 March 1981 (1981-03-31)

**2 INDEPENDENT CLAIM 1**

- 2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT. Document D1 discloses (the references in parentheses applying to this document):

A method of measuring an analyte (cf. abstract) based on multiple streams of optical radiation measured from a measurement site (cf. figure 2), said method comprising:  
emitting a sequence of optical radiation pulses to the measurement site (cf. abstract, page 7, lines 16-23) ;  
detecting at a first location (12a) a first stream of optical radiation from the measurement site;  
detecting at least at one additional location (12b) different from the first location an additional stream of optical radiation from the measurement site; and  
determining an output measurement value indicative of the analyte based on the

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/052756

detected streams of optical radiation (cf. abstract, page 8, lines 4-6) figure 2).

Hence, the subject-matter of claim 1 is disclosed in document D1.

- 2.2 Bearing in mind that an array of detectors allows detecting at a plurality of locations streams of optical radiation (cf. D1, page 8, lines 14-17), the subject-matter of claim 1 is disclosed also in documents D2-D5 (cf. the corresponding passages cited in the search report).

**3 INDEPENDENT CLAIM 7**

- 3.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 7 is not new in the sense of Article 33(2) PCT. Document D3 discloses (the references in parentheses applying to this document):

A front-end interface (4030) for a noninvasive, physiological sensor, said front-end interface comprising:

a set of inputs configured to receive signals (2500, cf. figures 7 and 40) from a plurality of detectors (cf. figures 2400, cf. paragraph 58, figures 25,26,40) in the sensor;

a set of transimpedance amplifiers (implicit: cf. paragraphs 72, 107) configured to convert the signals from the plurality of detectors into an output signal having a stream for each of the plurality of detectors; and

an output configured to provide the output signal (cf. figure 40).

**4 INDEPENDENT CLAIM 15**

- 4.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claim 15 does not involve an inventive step in the sense of Article 33(3)PCT.



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/052756

- 4.1.1 Document D2, discloses (cf. passages cited in the search report) a device from which the subject-matter of independent claim 15 differs in that:

the digital conversion is carried out by switched-capacitor circuits.

- 4.1.3 In document D2 no details are given about the circuits for A/D conversion. The problem to be solved by the present invention may therefore be regarded as to provide a specific embodiment of such circuits.

- 4.1.4 D6 discloses (cf. paragraph 42) switched-capacitor circuits for A/D conversion. The skilled person would therefore regard it as a normal option to include this feature in the device described in document D2, in order to solve the problem posed. The subject-matter of claim 15 thus cannot be considered inventive (Article 33(3) PCT).

**5 INDEPENDENT CLAIM 18**

- 5.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 18 is not new in the sense of Article 33(2) PCT. The subject-matter of claim 18 is just directed to the essential features of a processor unit having inputs signals from a detector array, said signals being converted in digital form and then processed by a signal processor. These essential features are disclosed in all documents D2-D4 (cf. the corresponding passages cited in the search report).

**6 INDEPENDENT CLAIM 25**

- 6.1 The same reasoning applies, mutatis mutandis, to the subject-matter of independent claim 25, which is just directed to the essential features of a multi-stream emitter and which is disclosed in all documents D2-D4 (cf. the corresponding passages cited in the search report), which therefore is therefore also considered not new (Articles 33(1) and 33(2) PCT).

**7 DEPENDENT CLAIMS 2-6, 8-14, 16, 17, 19-24, 26-36**

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference MLHUM.002VPC	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/US2009/052756	International filing date ( <i>day/month/year</i> ) 04 August 2009 (04.08.2009)	Priority date ( <i>day/month/year</i> ) 04 August 2008 (04.08.2008)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant MASIMO LABORATORIES, INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis.2).

	Date of issuance of this report 08 February 2011 (08.02.2011)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer  <b>Masashi Honda</b> e-mail: pt08.pct@wipo.int

Form PCT/IB/373 (January 2004)

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)Applicant's or agent's file reference  
see form PCT/ISA/220**FOR FURTHER ACTION**  
See paragraph 2 belowInternational application No.  
PCT/US2009/052756International filing date (day/month/year)  
04.08.2009Priority date (day/month/year)  
04.08.2008International Patent Classification (IPC) or both national classification and IPC  
INV. A61B5/00Applicant  
MASIMO LABORATORIES, INC.

## 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

## 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040  
Fax: +31 70 340 - 3016

Date of completion of  
this opinionsee form  
PCT/ISA/210

Authorized Officer

Ferrigno, Antonio

Telephone No. +31 70 340-2174



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/052756

---

**Box No. I Basis of the opinion**

---

1. With regard to the **language**, this opinion has been established on the basis of:
  - ☒ the international application in the language in which it was filed
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1 (a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ on paper
    - ☐ in electronic form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in electronic form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2009/052756

---

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

---

**1. Statement**

Novelty (N)	Yes: Claims	<u>8-17, 19-24, 28-30</u>
	No: Claims	<u>1-7, 18, 25-27, 31-36</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-36</u>
Industrial applicability (IA)	Yes: Claims	<u>1-36</u>
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/052756

**Re Item V.**

**1 Reference is made to the following documents:**

- D1 : WO 00/25112 A (ROLFE PETER [GB]) 4 May 2000 (2000-05-04)
- D2 : US 6816241 B2 (GRUBISIC DRAGAN [US] GRUBISIC DRAGAN [US] ET AL) 09 November 2004 (2004-11-09)
- D3 : US 2006/211924 A1 (DALKE DAVID [US] ET AL) 21 September 2006 (2006-09-21) cited in the application
- D4 : US 6 172 743 B1 (KLEY VIC [US] ET AL) 9 January 2001 (2001-01-09)
- D5 : US 5 676 143 A (SIMONSEN JAN HENNING [DK] ET AL) 14 October 1997 (1997-10-14)
- D6 : US 2004/049237 A1 (LARSON DENNIS E [US] ET AL) 11 March 2004 (2004-03-11)

US 4 258 719 A (LEWYN LANNY L) 31 March 1981 (1981-03-31)

**2 INDEPENDENT CLAIM 1**

- 2.1** The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT. Document D1 discloses (the references in parentheses applying to this document):

A method of measuring an analyte (cf. abstract) based on multiple streams of optical radiation measured from a measurement site (cf. figure 2), said method comprising:  
emitting a sequence of optical radiation pulses to the measurement site (cf. abstract, page 7, lines 16-23) ;  
detecting at a first location (12a) a first stream of optical radiation from the measurement site;  
detecting at least at one additional location (12b) different from the first location an additional stream of optical radiation from the measurement site; and  
determining an output measurement value indicative of the analyte based on the

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/052756

detected streams of optical radiation (cf. abstract, page 8, lines 4-6) figure 2).

Hence, the subject-matter of claim 1 is disclosed in document D1.

- 2.2 Bearing in mind that an array of detectors allows detecting at a plurality of locations streams of optical radiation (cf. D1, page 8, lines 14-17), the subject-matter of claim 1 is disclosed also in documents D2-D5 (cf. the corresponding passages cited in the search report).

**3 INDEPENDENT CLAIM 7**

- 3.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 7 is not new in the sense of Article 33(2) PCT. Document D3 discloses (the references in parentheses applying to this document):

A front-end interface (4030) for a noninvasive, physiological sensor, said front-end interface comprising:

a set of inputs configured to receive signals (2500, cf. figures 7 and 40) from a plurality of detectors (cf. figures 2400, cf. paragraph 58, figures 25,26,40) in the sensor;

a set of transimpedance amplifiers (implicit: cf. paragraphs 72, 107) configured to convert the signals from the plurality of detectors into an output signal having a stream for each of the plurality of detectors; and

an output configured to provide the output signal (cf. figure 40).

**4 INDEPENDENT CLAIM 15**

- 4.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claim 15 does not involve an inventive step in the sense of Article 33(3)PCT.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/052756

- 4.1.1 Document D2, discloses (cf. passages cited in the search report) a device from which the subject-matter of independent claim 15 differs in that:

the digital conversion is carried out by switched-capacitor circuits.

- 4.1.3 In document D2 no details are given about the circuits for A/D conversion. The problem to be solved by the present invention may therefore be regarded as to provide a specific embodiment of such circuits.

- 4.1.4 D6 discloses (cf. paragraph 42) switched-capacitor circuits for A/D conversion. The skilled person would therefore regard it as a normal option to include this feature in the device described in document D2, in order to solve the problem posed. The subject-matter of claim 15 thus cannot be considered inventive (Article 33(3) PCT).

**5 INDEPENDENT CLAIM 18**

- 5.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 18 is not new in the sense of Article 33(2) PCT. The subject-matter of claim 18 is just directed to the essential features of a processor unit having inputs signals from a detector array, said signals being converted in digital form and then processed by a signal processor. These essential features are disclosed in all documents D2-D4 (cf. the corresponding passages cited in the search report).

**6 INDEPENDENT CLAIM 25**

- 6.1 The same reasoning applies, mutatis mutandis, to the subject-matter of independent claim 25, which is just directed to the essential features of a multi-stream emitter and which is disclosed in all documents D2-D4 (cf. the corresponding passages cited in the search report), which therefore is therefore also considered not new (Articles 33(1) and 33(2) PCT).

**7 DEPENDENT CLAIMS 2-6, 8-14, 16, 17, 19-24, 26-36**



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/052756

- 7.1 The additional features of dependent claims 2-6, 26, 27, and 31-36 are disclosed in at least one of the documents D1-D5 (cf. the corresponding passages cited in the search report) and therefore the subject-matter of these claims is not new.
- 7.2 The additional features of dependent claims 8-14, 16, 17, 19-24, and 28-30 are just some of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill.

CX-1621

<b>Electronic Acknowledgement Receipt</b>	
<b>EFS ID:</b>	11264234
<b>Application Number:</b>	12534827
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	1308
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	20995
<b>Filer:</b>	Jarom D. Kesler/Erica Van Sciver
<b>Filer Authorized By:</b>	Jarom D. Kesler
<b>Attorney Docket Number:</b>	MLHUM.002A
<b>Receipt Date:</b>	25-OCT-2011
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<b>Time Stamp:</b>	19:34:34
<b>Application Type:</b>	Utility under 35 USC 111(a)

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**File Listing:**

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		IDS_MLHUM_002A.PDF	72542 f93f07fbc8a1c6866f1060e7f3fee02cdb17c83	yes	2

CX-1621

Multipart Description/PDF files in .zip description					
Document Description			Start	End	
Transmittal Letter			1	1	
Information Disclosure Statement (IDS) Form (SB08)			2	2	
<b>Warnings:</b>					
<b>Information:</b>					
2	Foreign Reference	WO_00_025112.PDF	959184	no	25
			6d973a89434b07869f6334035cd433d850762b07		
<b>Warnings:</b>					
<b>Information:</b>					
3	Non Patent Literature	ISR_MLHUM002VPC.PDF	579672	no	14
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<b>Warnings:</b>					
<b>Information:</b>					
4	Non Patent Literature	IPRP_MLHUM002VPC.PDF	276902	no	8
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<b>Warnings:</b>					
<b>Information:</b>					
<b>Total Files Size (in bytes):</b>			1888300		
<p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b>  If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b>  If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b>  If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>					

Docket No.: MLHUM.002A

Customer No. 20995

**INFORMATION DISCLOSURE STATEMENT**

Applicants : Poeze, et al.  
App. No : 12/534,827  
Filed : August 3, 2009  
For : MULTI-STREAM DATA  
COLLECTION SYSTEM FOR  
NONINVASIVE MEASUREMENT OF  
BLOOD CONSTITUENTS  
Examiner : Winakur, Eric Frank  
Art Unit : 3768  
Conf No. : 1308

**CERTIFICATE OF EFS WEB  
TRANSMISSION**

I hereby certify that this correspondence, and any other attachment noted on the automated Acknowledgement Receipt, is being transmitted from within the Pacific Time zone to the Commissioner for Patents via the EFS Web server on:

October 25, 2011

(Date)

/Jarom Kesler/

Jarom D. Kesler, Reg. No. 57,046

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed for filing in the above-identified application is a PTO/SB/08 Equivalent listing 8 references, of which 3 are enclosed/submitted.

This Information Disclosure Statement is being filed before the receipt of a first Office Action on the merits, and presumably no fee is required. If a first Office Action on the merits was mailed before the mailing date of this Statement, the Commissioner is authorized to charge the fee set forth in 37 C.F.R. § 1.17(p) to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON &amp; BEAR, LLP

Dated: October 25, 2011

By: /Jarom Kesler/  
Jarom D. Kesler  
Registration No. 57,046  
Attorney of Record  
Customer No. 20995  
(949) 760-0404

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PTO/SB/08 Equivalent

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

	Application No.	12/534,827
	Filing Date	August 3, 2009
	First Named Inventor	Poeze, et al.
	Art Unit	3768
	Examiner	Unknown
(Multiple sheets used when necessary)	Attorney Docket No.	MLHUM.002A
SHEET 1 OF 1		

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	4,267,844	05/19/1981	Yamanishi	
	2	4,655,225	04/07/1987	Dähne, et al.	
	3	4,781,195	11/01/1988	Martin	
	4	4,805,623	02/21/2989	Jöbsis	
	5	5,028,787	07/02/1991	Rosenthal, et al.	
	6	5,077,476	12/31/1991	Rosenthal	
	7	5,137,023	08/11/1992	Mendelson, et al.	
	8	5,337,745	08/16/1994	Benaron	

## FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>
	9	EP419223	03/27/1991	Minnesota Mining and Manufacturing Company		

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	10	Burritt, Mary F.; Current Analytical Approaches to Measuring Blood Analytes; Vol. 36; No. 8(B); 1990	
	11	Hall, et al., Jeffrey W.; Near-Infrared Spectrophotometry: A New Dimension in Clinical Chemistry; Vol. 38; No. 9; 1992	
	12	Kuenstner, et al., J. Todd; Measurement of Hemoglobin in Unlysed Blood by Near-Infrared Spectroscopy; Vol. 48; Number 4, 1994	
	13	Manzke, et al., B., Multi Wavelength Pulse Oximetry in the Measurement of Hemoglobin Fractions; Vol. 2676	
	14	Naumenko, E. K.; Choice of Wavelengths for Stable Determination of Concentrations of Hemoglobin Derivatives from Absorption Spectra of Erythrocytes; Vol. 63; No. 1; pp. 60-66 January - February 1996; Original article submitted November 3, 1994	
	15	Schmitt, Joseph M.; Simple Photon Diffusion Anaylsis of the Effects of Multiple Scattering on Pulse Oximetry; March 14, 1991; revised August 30, 1991	
	16	Schmitt, et al., Joseph M.; Measurement of Blood Hematocrit by Dual-Wavelength near-IR Photoplethysmography; Vol. 1641; 1992	
	17	Schnapp, et al., L.M.; Pulse Oximetry. Uses and Abuses.; Chest 1990; 98; 1244-1250 DOI 10.1378/Chest.98.5.1244	

3309546

Examiner Signature	Date Considered
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\***Examiner:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

CX-1621

Electronic Acknowledgement Receipt	
EFS ID:	8194892
Application Number:	12534827
International Application Number:	
Confirmation Number:	1308
Title of Invention:	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
First Named Inventor/Applicant Name:	Jeroen Poeze
Customer Number:	20995
Filer:	Jarom D. Kesler/Valerie Jones
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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	EP0419223A2.pdf	3002370 177d9288ef92992d659539a08cda01726aff14b	no	51

**Warnings:****Information:**

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2	NPL Documents	npl10.pdf	569626	no	5
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Information:					
3	NPL Documents	npl11.pdf	823239	no	9
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8	NPL Documents	npl16.pdf	742243	no	12
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Warnings:					
Information:					
9	NPL Documents	npl17.pdf	791352	no	9
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10		002a.pdf	114298	yes	2
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Multipart Description/PDF files in .zip description			
Document Description	Start	End	
Transmittal Letter	1	1	
Information Disclosure Statement (IDS) Filed (SB/08)	2	2	

**Warnings:**

**Information:**

<b>Total Files Size (in bytes):</b>	9481946
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**This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.**

**New Applications Under 35 U.S.C. 111**  
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

**National Stage of an International Application under 35 U.S.C. 371**  
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**  
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.





Publication number: **0 419 223 A2**

**EUROPEAN PATENT APPLICATION**

Application number: **90310219.2**

Int. Cl.<sup>5</sup>: **G01N 21/35, G01N 33/48,  
G06F 15/20, G06F 15/336**

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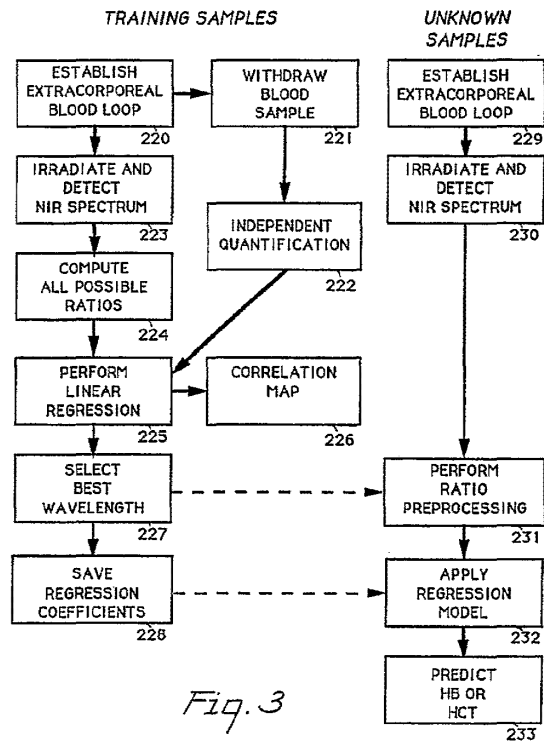
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**Characterizing biological matter in a dynamic condition using near infrared spectroscopy.**

A method is provided for predicting a property of a matter of biological origin, such as biological fluid, containing water, in a dynamic condition where the biological fluid may be approximated to contain two compartments where one compartment has a proportionally larger or smaller amount of water than the other compartment having the property of interest. The method involves establishing a training set in the near-infrared (NIR) region with independent quantification of the property of the fluid using known techniques. The training set is mathematically analyzed according to a correlation developed by regression analysis after employment of a pre-processing technique such as a multiple derivative transformation of spectra or a ratioing of two wavelengths in the spectra. The result is a mathematical transformation equation which quantitatively relates spectral intensities at specific wavelengths to the property of interest. This transformation equation may be applied to unknown samples so as to predict their properties, thereby eliminating need for the reference method except for validation or recalibration. The method provides rapid and accurate prediction of the property of the unknown sample, which may be the property of hematocrit or hemoglobin concentration in whole animal blood. Other analyses of properties in the biological fluid such as oxygen saturation in hemoglobin in whole animal blood may be included in the mathematical analysis to further refine the prediction of the property of interest. Also, a loop from the patient is disclosed for the purpose of monitoring the property of interest nearly simultaneously with changes in that property of interest.

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**CHARACTERIZING BIOLOGICAL MATTER IN A DYNAMIC CONDITION USING NEAR INFRARED SPECTROSCOPY**Field of the Invention

5 The present invention relates to the analysis of a sample of matter of biological origin in a dynamic condition using the near infrared (NIR) spectrum of that biological matter having a water content. The method permits prediction of a property of interest because the biological matter may be approximated to contain two compartments where one compartment has a proportionally larger or smaller amount of water than the other compartment having the property of interest. Analysis of an unknown sample in a dynamic condition is achieved by use of mathematical techniques developed using a NIR spectral training set of  
 10 known samples and independent quantification of the property of interest in the known samples in that training set.

Background of the Invention

15

Presence of water in an organism is the common denominator of life. The corpus of an organism is compartmentalized with each compartment capable of being distinguished by the amount of water it contains. The processes of osmosis and reverse osmosis in an organism act to stabilize this compartmentalization.  
 20

Determination of the volume fraction or percentage concentration of components other than water in the various compartments of biological matter, such as tissue or blood, is often critical to the determination of the well-being or homeostasis of the organism. Whether in the botanical, medical, zoological or veterinary arts, because the circulation of biological fluid or existence of certain biological tissue in an organism is necessary for life, the diagnosis of such biological matter provides an excellent medium to assess the  
 25 homeostatic condition of the organism.

Blood of animals circulates essential nutrients of life. Erythrocytes, red blood cells, flowing in the blood plasma carry oxygen to all other cells of the organism. Hematocrit is the volume fraction of agglomerated erythrocytes in whole blood. Hemoglobin is the chemical molecule in the erythrocytes which transports  
 30 oxygen to the cells. Hemoglobin may take several forms depending on the presence or absence of oxygen or other chemicals which may be bonded to active sites in the hemoglobin molecule. Hematocrit in whole blood has been found to have a suitable direct mathematical correlation to the concentration of hemoglobin, providing the blood has few or no lysed erythrocytes.

Water is omnipresent in whole blood. Hemoglobin is dissolved in the erythrocytes, while plasma is principally water. But the amount of water in which hemoglobin is dissolved, and hence in erythrocytes, is comparatively less than the amount of water in the plasma.  
 35

Clinical analysis of an organism requires monitoring of the status of or the changes in condition. As a result of injury or illness or other deleterious biological conditions, the hematocrit or the concentration of hemoglobin in erythrocytes available for oxygen transport to the cells of the organism may be diminished below healthy levels even to the point of critical life sustaining levels. Also, analysis of various types of anemia is vital to continuing successful treatment of a patient, especially in critical care facilities such as emergency rooms, operating rooms, or intensive care units, including neo-natal units. Less traumatic but just as vital, most blood donors must undergo hematocrit testing to assure that their blood to be donated has appropriate hemoglobin levels for later use.  
 40

Several types of techniques have been known for the analysis of blood during patient care. Hemoglobin concentrations are measured traditionally using lengthy and complicated procedures which require the preconditioning, i.e., chemical modification or component separation, of a blood sample withdrawn from the body. The traditional methods destroy the blood, preventing its return to the body.  
 45

One popular method for the determination of hemoglobin involves (1) lysing the red blood cells by hypotonic shock or sonification, (2) removal of the red blood cell membranes to produce a clear solution, (3) addition of a cyanide ion reagent to normalize or convert the various forms of hemoglobin to a single form hemoglobin (e.g., cyanomet hemoglobin), and (4) spectrophotometric analysis to derive the hemoglobin concentration of the normalized sample.  
 50

Because of the complicated chemical procedure for determination of hemoglobin concentration, and

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because of the known direct correlation between hematocrit and hemoglobin concentration, methods for independently determining hematocrit have been developed.

The most common methods for measurement of hematocrit can be divided into two categories: centrifugal attribution in a test tube of specific diameter and Coulter counting.

5 Centrifugal attribution involves centrifuging of blood withdrawn from the body in a tube of specific diameter at pre-selected centrifugal forces and times that serve to separate the blood into two portions. The heavier portion is the agglomeration of erythrocytes in the whole blood. The lighter portion is plasma dominated by water. The ratio of the volume of the erythrocytes to the total volume of the blood sample in the centrifuge tube is the hematocrit.

10 Coulter counting determines hematocrit by physical counting of red blood cells and a determination, through the size of each cell on a cell-by-cell basis, the volume of each. After a predetermined number of blood cells are counted, the hematocrit is determined by the number of red blood cells counted multiplied by the mean volume of the blood cells for a given blood sample.

As may be understood by considering such current methods, considerable manipulation and laboratory analysis is necessary for each individual blood sample drawn from the body of the patient. Whether 15 measuring hematocrit or hemoglobin concentration, the blood sample is withdrawn from the patient and inevitably taken from the immediate vicinity of the patient for analysis using expensive, stationary instrumentations that require preconditioning of the sample in order to analyze it.

Efforts to spectrally analyze blood samples for hematocrit or hemoglobin concentration have been 20 attempted. U.S. Patent 4,243,883 describes a monitor of a flowing stream of blood using a discrete near-infrared wavelength. U.S. Patent 4,745,279 describes a dual path NIR spectral analysis at discrete wavelengths of flowing whole blood. U.S. Patent 4,805,623 describes a NIR spectral method and apparatus using multiple wavelengths to determine the concentration of a dilute component of known identity in comparison with a reference component of known concentration.

25 The near-infrared (NIR) spectral region of electromagnetic radiation, from about 680 nanometers to 2700 nanometers, contains absorbance peaks for the various forms of hemoglobin and water. Prior spectral analytical efforts have focused on the measurement of the diffuse transmission or reflectance of near infrared light through blood samples. However, light scattering in the samples and other properties which interfere with accurate measurement cause variances in the specific spectrum taken. As a result, even using 30 measurements taken with sensitive instrumentation is not satisfactory. Moreover, the choice of specific wavelengths in near-infrared spectra for which whole blood samples may be best monitored is not straightforward due to variances in the broad peaks of water and various forms of hemoglobin in such NIR spectra.

Even with the best monitoring wavelengths being chosen, one must address the variability caused by 35 the effective path length that the transmitted or reflected near-infrared radiation takes between excitation and detection through the blood sampling. This is especially true when the blood being irradiated is constantly changing due to movement of the blood, a dynamic condition for spectral analysis. Prior efforts to employ NIR spectral analysis have either discounted the importance of determining effective path length or required procedures to establish the effective path length prior to completing the spectral analysis. In the 40 former case, reproducible precision suffers; in the latter case, a complicated methodology is employed.

Thus, what is needed is a method for accurately determining through NIR spectral analysis in a dynamic condition a property of a sample of biological matter which is rapid, inexpensive, accurate, precise, and which takes into account such spectroscopic variabilities as effective path length of the reflected or transmitted light or where instrumentation may be using either a continuous measurement of absorbance 45 wavelengths across a NIR spectra or at discrete wavelengths thereof.

#### Summary of the Invention

50 The present invention provides a method for rapidly, inexpensively, and accurately characterizing the properties of matter of biological origin containing water by analyzing the near-infrared spectrum of the biological matter while in a dynamic condition using techniques useful with NIR spectral instrumentation and predicting the properties without sample preconditioning. The techniques seek to minimize the effect of light 55 scattering and use mathematical regression analysis to permit transforming the observed spectrum into a prediction of the property to be analyzed.

The method of the present invention avoids chemical alteration or physical separation of the components in the sample of biological matter. The method also avoids inaccuracies caused by irrelevant

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variations in samples and instrumental noise in measurement techniques.

The method of the present invention is founded on the principle that the biological matter may be considered to consist of essentially two compartments: one compartment which has a proportionally different (larger or smaller) amount of water than the other compartment related to or having the property to be analyzed. The present invention is also founded on the principle that identification of the volume or weight fraction or concentration of water in the biological matter will serve as the basis for calculation of the property to be analyzed. The method of the present invention is further founded on the principle that the establishment of a training set of the combination of NIR spectra of several samples of the biological matter and the independent quantification of the property to be analyzed in each sample provides a source of mathematical comparison for accurately predicting the property to be analyzed in an unknown additional sample by using such mathematical comparison.

When the biological matter is whole blood, prediction of the hematocrit or hemoglobin concentration is achieved by obtaining near-infrared spectra of a statistically sufficient number of samples of whole blood to establish a training set for mathematical comparisons against individual additional unknown samples of other whole blood. Further, the property to be analyzed in the whole blood, e.g., hematocrit or hemoglobin concentration, is independently quantified by using an independent known technique: lysing and chemical alteration for hemoglobin and Coulter counting or centrifuging for hematocrit.

Having established a training set of NIR spectra and independently quantified the hematocrit or hemoglobin concentration in each sample in the training set, the nature of the inter-relationship between the hematocrit or hemoglobin and the water content is statistically correlated to establish the source of comparison when predicting unknown samples.

To minimize variability when establishing the training set and when predicting the properties of the compartment being analyzed in the unknown sample, a pre-processing technique is employed.

One useful pre-processing technique is disclosed in European Patent Publication based on an application claiming priority from U.S. Patent Application Serial Number 07/408,747. That technique is a multiple derivative transformation of the training set spectra and the unknown sample's spectrum to minimize the effect of light scattering and other instrumental noise on the various spectra, in order to allow a mathematical correlation using the multiple derivative of the spectral intensity at a single wavelength to accurately predict the property of the compartment being analyzed in the unknown sample.

A different and useful type of pre-processing technique is disclosed in European Patent Publication based on an application claiming priority from U.S. Patent Application serial Number 07/408,746. That technique is a ratio pre-processing technique which applies a ratio of an absorbance peak of the water content in the biological matter to another absorbance measuring point in order to minimize variations due to sampling techniques and instrumentation factors. This allows the accurate mathematical correlation to predict the property of the compartment being analyzed in the unknown sample.

In the case of hematocrit or hemoglobin concentration determinations, through mathematical regression analysis, it has been found that use of the absorbance peak of water appearing in NIR spectra in the range of from about 1150 to about 1190 nanometers (nm) provides an accurate and reproducible peak for multiple derivative transformation pre-processing techniques, notwithstanding a known decrease in detector efficiency using silicon detectors in this range of wavelengths. This peak of absorbance of water in the 1150-1190 nm range is largely isolated from the absorbance of hemoglobin either in its oxygenated state or in its deoxygenated state. The absorbance peak of water in this region is primarily the result of simultaneous excitation of the symmetric O-H stretch, the O-H bending mode, and the antisymmetric O-H stretch of the water molecule, whether existing in the biological matter as free water, bound to other molecules, or other forms.

While the peak of absorbance of water in the 1150-1190 nm range may be largely isolated from the absorbance of hemoglobin, it is not totally isolated. Indeed, it is preferred in the present invention to distinguish between the two principal forms of the hemoglobin component in whole blood, oxyhemoglobin and deoxyhemoglobin, and add that independent variable to the regression analysis which both establishes the training set and predicts the unknown sample's hematocrit or hemoglobin concentration.

Gathering the training set spectral data for the samples of the biological matter depends on the type of instrumentation to be employed. To establish the training set according to the present invention, the biological matter is diverted from the body of the organism and returned.

For purposes of full disclosure, a different and useful method of gathering data employing a static condition of spectral analysis is disclosed in either European Patent Publication or European Patent Publication based on applications claiming priority from U.S. Patent Application Serial Number 07/408,747 or U.S. Patent Application Serial Number 07/408,746, respectively. In those instances the biological matter may be withdrawn from the body of the organism. Additionally, the biological matter may

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be measured within the body of the organism. However, to provide the independent quantification of the property to be analyzed from the training set samples, a sample of the biological matter must be withdrawn from the organism and often cannot be returned to the organism because of chemical alteration or physical separation of the compartment in the matter.

5 One embodiment of diversion and return of the biological matter to the patient is an extracorporeal loop described herein.

Gathering the unknown sample spectral data for analysis also depends on the type of instrumentation to be employed. The unknown sample may be diverted from the body of the organism for spectral detection or measurement and returned to the body, or the unknown sample may be analyzed in vivo. One  
10 embodiment of diversion and return of the biological matter to the patient is the extracorporeal loop described herein.

Processing and instrumentation variabilities are dependent upon the method by which the training set is established and the method by which the unknown samples are analyzed. In the present invention, the biological fluid is moving when being spectrally analyzed, a dynamic condition.

15 When the biological fluid is whole blood and the hematocrit or the concentration of hemoglobin is desired, the whole blood, either moving from the body through a optical path before returning or moving in the body, is spectrally analyzed in a dynamic condition either using diffuse transmission detection or reflectance detection as appropriate.

Because of the use of the appropriate pre-processing technique, variations due to sampling techniques  
20 of biological matter in a dynamic condition and instrumentation factors such as effective path length are minimized.

The NIR spectrum of the unknown sample is obtained from either continuous or discrete wavelength measuring instrumentation. After the spectrum is obtained and subjected to the appropriate pre-processing, the property of interest may be predicted by a mathematical correlation to the training set spectra.

25 In the case of the measurement of hematocrit or hemoglobin concentration in an unknown sample of whole blood, after the NIR spectrum of the unknown sample is observed and subjected to pre-processing, application of mathematical techniques comparing the training set spectral data for the hematocrit or the hemoglobin concentration with the unknown sample's spectra allows prediction of the hematocrit or the hemoglobin concentration in the unknown sample.

30 For an additional appreciation of the scope of the present invention, a more detailed description of the invention follows, with reference to the drawings.

#### Brief Description of the Drawings

35 FIG. 1 is a schematic block diagram of the instrumentation useful in a method carried out in accordance with the present invention.

FIG. 2 is a schematic flow chart of the methods to mathematically minimize variability of spectral data using multiple derivative transformation techniques and establish the mathematical correlation between  
40 known samples and the training set spectra, in order to permit the predicting of the property of interest in an unknown sample by comparison with the mathematical correlation.

FIG. 3 is a schematic flow chart of the methods to mathematically minimize variability of spectral data using ratioing techniques and establish the mathematical correlation between known samples and the training set spectra, in order to permit the predicting of the property of interest in an unknown sample by  
45 comparison with the mathematical correlation.

FIG. 4 is a graphic representation of typical whole blood spectra detected in a dynamic condition indicating the effects of typical light scattering variances and other instrumental noise variances.

FIG. 5 is a graphic representation of the same whole blood spectra as in FIG. 4 after the application of the multiple derivative transformation to minimize the effects of typical light scattering variances and  
50 other instrumental noise variances.

FIG. 6 is a correlation plot of correlation coefficient versus wavelength for hemoglobin after the spectral data were second derivative pre-processed and regression analysis of the spectral data was performed against hemoglobin.

FIG. 7 is a correlation map of correlation coefficient squared versus wavelength for hemoglobin after ratio  
55 pre-processing and regression analysis of the spectral data was performed against hemoglobin.

FIG. 8 is a graph showing the accuracy of prediction of hematocrit after multiple derivative transformation pre-processing compared with actual hematocrit values determined by prior art methods.

FIG. 9 is a graph showing the accuracy of prediction of hematocrit after ratioing pre-processing

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compared with actual hematocrit values determined by prior art methods.

FIG. 10 is a schematic flow chart, similar to FIG. 2, of another method of the present invention to mathematically minimize variability of spectral data using multiple derivative transformation techniques and adjustment for the different forms of hemoglobin.

5 FIG. 11 is a schematic flow chart, similar to FIG. 2, of another method of the present invention to mathematically minimize variability of spectral data using ratioing techniques and adjustment for the different forms of hemoglobin in the whole blood.

FIG. 12 is a graph showing the accuracy of prediction of hematocrit after multiple derivative transformation pre-processing and adjusting for the different forms of hemoglobin present in the whole blood, compared with actual hematocrit values determined by prior art methods.

10 FIG. 13 is a graph showing the accuracy of prediction of hematocrit after ratioing pre-processing and adjusting for the different forms of hemoglobin present in the whole blood, compared with actual hematocrit values determined by prior art methods.

FIG. 14 is a schematic depiction of the components of the extracorporeal blood loop of the present invention.

### Embodiments of the Invention

One embodiment of the present invention is the analysis of hematocrit in whole blood. Another  
20 embodiment of the present invention is the analysis of hemoglobin concentration in whole blood. There are occasions when either analysis may be preferred. But generally, it is recognized that the determination of hematocrit is an excellent correlation to the concentration of hemoglobin in whole blood. However for versatility of the system, it should be recognized that one or more methods of independent quantification of the property to be analyzed may be used to provide alternative clinical diagnosis of the condition of the patient.

It should also be recognized that the property of the biological matter to be analyzed must have some correlation either positively or negatively with the water content in order to develop a mathematical correlation therefor in accordance with the present invention. That may not preclude the presence of other components in de minimus volume fractions or concentrations. For example, in whole blood, the presence  
30 of white blood cells, platelets, hydrocarbonaceous lipids, and the like are not present in sufficient quantity at the desired level of precision to destroy the validity of the mathematical correlation found. However, as described below, the determination of the oxygen saturation in the whole blood may distinguish between oxyhemoglobin and deoxyhemoglobin, in order to predict the property of interest with greater accuracy.

### SPECTROSCOPIC INSTRUMENTATION

FIG. 1 identifies the schematic block diagram of spectral instrumentation useful in establishing the  
40 training set initially and thereafter predicting the property of the compartment to be analyzed in one or more unknown additional samples.

FIG. 1 illustrates a typical instrumentation system available which can be used for obtaining the near infrared spectrum of a biological fluid, such as whole blood. Specifically, FIG. 1 identifies a Model 6250 spectrophotometer manufactured by Near Infrared Systems of Silver Spring, Maryland, formerly known as  
45 Model 6250 made by Pacific Scientific. The radiation from a tungsten lamp 100 is concentrated by a reflector 101 and lens 102 on the entrance slit 103 and thereafter passed through an order sorting filter 104 before illuminating a concave holographic grating 105 to disperse the radiation from the tungsten lamp 100 onto the sample 113 in a dynamic condition in an optical blood loop or in the body of the organism. The grating 105 is where the wavelength dispersion occurs. The grating is scanned through the desired  
50 wavelength range, typically 680 to 1235 nanometers, by the rotating cam bearing 106, which is coupled to the grating by linkage assembly 107. The selected wavelength passes through exit slit 108 and is guided through the cell 113 through which the sample is moving in direction F, by mirror 109, iris 111, and lenses 110 and 112. After passing through the sample, the remaining radiation is converted to an electrical signal by detector 114.

55 Other types of instrumentation are also acceptable for use with the methods of the present invention. Monochromators such as Model HR 320 available from Instruments S.A. are useful. Polychromators such as the Chemspec Model 100S available from American Holograph or Model JY320 also available from Instruments S.A. may be used to gather the spectral data to establish the training set.

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Detection means may employ either diffuse transmittance detection devices or reflectance devices available commercially. The Model 6250 spectrophotometer may be configured to detect either diffuse transmittance or diffuse reflectance. Depending on factors such as cost, wavelength range desired, and the like, the detector 114 may be a silicon detector, a gallium arsenide detector, a lead sulfide detector, an indium gallium arsenide detector, a selenium detector or a germanium detector.

Whichever detector is chosen, it is preferred to be consistent in the usage of same detection means for establishing the training set spectra and for measuring the unknown sample's spectrum.

Alternately, polychromatic analyzers using a reversed beam geometry may be used to disperse the transmitted or reflected light into its spectral components and photodiode arrays may be used to detect or measure the dispersed light at different positions along the output spectral plane.

Other types of array detectors include charge coupled devices, charge injection devices, silicon target vidicons, and the like. Desirably, the polychromatic analyzer should include an entrance slit that defines the bandwidth of light which is consistent with the spectral resolution desired. One commercially available photodiode array useful with the present invention is Model 1024S photodiode array available from Reticon, Inc., which consists of 1024 diodes of 25 micron width and 2.5 millimeters height. That photodiode array may be used in a complete spectral detection system such as Model ST120 available from Princeton Instruments.

One can also use interference filters as spectroanalyzers, for example, by passing a series of discrete wavelength interference filters one at a time before a suitable detector. It is also possible to use interferometers or a Hadamard transform spectrometer to analyze the diffuse light.

The above detection means are based on detection of spectra from a broad band light source. However, if narrow band sources of NIR light are to be used, such as tungsten lamps with interference filters, light emitting diodes, or laser (either a single tunable laser or multiple lasers at fixed frequencies), other detection techniques may be used. For example, the input signal can be multiplexed either in time, (to sequence each wavelength), or in wavelength (using sequences of multiple wavelengths), and thereafter modulated and the collected signals demodulated and demultiplexed to provide individual wavelength signals without the need for optical filtering.

Regardless of the spectroscopic instrumentation selected, it is preferred to use a computer connected to the instrument to receive the spectral data, perform the analysis described below, and provide a printout or readout of the value of the property predicted. When using spectrometric instruments such as the Model 6250 spectrometer described above, a personal computer such as a "PS/2" Model 50 computer from IBM of Boca Raton, Florida is used and preferred.

#### MULTIPLE DERIVATIVE PRE-PROCESSING TECHNIQUE AFTER DYNAMIC CONDITION SPECTRAL DATA GATHERING

FIG. 2 is a schematic flow chart of the method of the present invention using for pre-processing the multiple derivative transformation pre-processing technique disclosed in U.S. Patent Application Serial Number 07/408,747, which pre-processing is employed to minimize sample and instrumentation variability. The regression analysis of the method identifies the nature of the mathematical correlation between the property to be analyzed in the first compartment and the water content in the biological matter, in order to predict the property of the compartment to be analyzed in an unknown sample.

The schematic flow of the processing steps involved in determining the property of interest in the biological matter, such as hematocrit or hemoglobin concentration, can be broadly divided into two parts: steps 120 to 128 which comprise the training phase of the analysis and steps 129 to 133 which comprise the prediction of the property of an unknown sample.

The training or calibration development phase consists of observing a series of blood samples 120 by diverting the samples from one or more animals of the same species through a blood loop or by otherwise observing the samples in the organisms. Additionally, for the independent quantification of property of interest, samples are obtained by withdrawing blood, step 121, from each of the animals participating in step 120.

The samples of steps 120 and 121 are analyzed on two parallel paths.

The first path consists of independent quantification of the property of interest, step 122. It is important that the independent quantification be done accurately. The accuracy of the method of the present invention is dependent upon the accuracy of the independent quantification step 122 because validation of the mathematical correlation is based on the independently quantified value of the property of interest.



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The second path consists of irradiating the samples with infrared light and detecting the near infrared spectrum for each sample, step 123, and then computing the second derivative of the spectra, step 124. It should be understood that reference to detecting the near infrared spectrum involves both the measurement of diffusely transmitted or reflected spectrum and the transformation of that spectrum to an absorbance spectrum. The transformation is based on having taken a spectrum of the cell containing only air for calibration purposes.

When the near infrared spectrum has been detected on a Near Infrared Systems Model 6250 spectrophotometer, the near infrared spectrum from 680 to 1235 nanometers consists of 700 individual absorbance measurements. The second derivative transformation preprocessing step computes less than the total 700 measurements because some transformations are not available at the edges of the spectra. When using software such as "Near Infrared Spectral Analysis" commercially available from Pacific Scientific, now known as Near Infrared Systems of Silver Spring, Maryland, one may compute an approximated derivative by using finite difference approximations. Different approximations may yield different derivative spectra and different transformation equations. In such software, different approximations may be adjusted according to segment of the spectrum being measured and the gap between segments being measured. Using different derivative approximations may result in a different set of regression coefficients that may affect the accuracy or precision of the prediction of the property being analyzed. It is therefore prudent to evaluate a wide range of segments and gaps in order to ascertain which selection is best for the particular analysis contemplated.

The preprocessed spectra for the set of training samples subjected to second derivative transformation, step 124, are correlated with the values obtained during the independent quantification step 122 by using a mathematical regression technique, step 125, such as linear regression. The second derivative value providing the best correlation of calculated value to actual value is generally the wavelength chosen for the mathematical correlation.

One of the outputs of this regression step is a correlation plot, step 126, which graphically shows the wavelengths of the spectrum where the highest correlation is found. The best transformed wavelength in the water band region of 1150 to 1190 nm, step 127, is selected by identifying the peak of optimum correlation. The regression coefficients corresponding to the selected wavelength are saved, step 128, for future application to the analysis of individual samples to predict the property of interest.

The steps 129 to 133 in FIG. 2 show the procedure to be followed for predicting hematocrit (abbreviated as HCT in FIG. 2) or hemoglobin (abbreviated as HB in FIG. 2) concentration in an individual unknown sample. A blood sample of unknown hematocrit or hemoglobin concentration, step 129, is observed by viewing the blood in an extracorporeal blood loop or in the organism, and the near infrared spectrum of this sample is detected or measured, step 130.

While the near infrared spectrum of additional unknown samples may also be detected on exactly the same instrument as the training samples were detected and from which the training set is prepared, it is also acceptable to use a simpler instrument which will provide the absorbance at only the three minimal wavelengths necessary to compute a second derivative transformation of the best wavelength.

The second derivative intensity for the best wavelength determined in step 127 is computed for the unknown sample, step 131. Then the regression coefficients contained in the mathematical correlation, determined during the training procedure and saved in step 128, are applied to the second derivative wavelength obtained for the additional individual unknown blood sample 132, in order to yield the predicted hematocrit or hemoglobin concentration, step 133.

The pre-processing technique of multiple derivative transformation serves to eliminate the variances of spectral data caused by scatter in each of the various samples of both the training set and each unknown sample. This scatter would otherwise disrupt the accuracy of the detection of the training set spectra and its ability to predict the property of the unknown sample.

If the near infrared spectrum consists of N individual wavelengths, computing the second derivative transformation provides N spectral features less the loss of the features at the edges of the spectrum. In FIG. 2, such computation is shown at step 124. The best wavelength must be chosen from the myriad of N transformed wavelengths using regression mathematical techniques, as is shown in FIG. 2 at step 125, depicted in a correlation plot at step 126, and selected at step 127 for use to determine the best possible regression coefficients in step 129 and for use with each unknown sample in step 132.

Any of a number of regression techniques; such as, linear regression, multiple linear regression, stepwise regression, partial least squares regression, or principal component regression can be used to develop a statistical correlation between the ratio spectral features and the variable of the property being quantified. Such regression techniques are available by reference to such literature as Draper and Smith, Applied Regression Analysis, Wiley and Sons, New York, 1982 and Geladi and Kowalski, Analytica Chimica

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Acta, Volume 185, pp 1-17 and 19-32, 1986.

In order to determine the best wavelength for a given application, regression models are computed against all of the possible N transformed wavelengths.

Each regression model is evaluated by using an accepted statistical measure. For example, one useful  
5 measure is the simple correlation coefficient computed from the actual hematocrit value obtained from the independent quantification and the predicted hematocrit value obtained from the regression model, as is shown in FIG. 2 at step 127.

A correlation plot can be constructed to visually show which wavelength involving the absorbance of water provides the highest correlation, as is shown in FIG. 2 at step 127. A representative correlation plot  
10 for hemoglobin appears as FIG. 6. It is important to consider both high correlation and also the sensitivity of the correlation obtained to measure small changes in the actual wavelengths.

## RATIO PRE-PROCESSING TECHNIQUE AFTER DYNAMIC CONDITION SPECTRAL DATA GATHERING

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FIG. 3 is a schematic flow chart of the method of the present invention using for pre-processing the ratio pre-processing technique described herein and also disclosed in U.S. Patent Application Serial Number 07/408,746, which pre-processing is employed to minimize sample and instrumentation variability.  
20 The regression analysis of the method identifies the nature of the mathematical correlation between the property to be analyzed in the first compartment and the water content in the biological matter, in order to predict the property to be analyzed in an unknown sample.

The schematic flow of the processing steps involved in determining the property of interest in the biological matter, such as hematocrit or hemoglobin concentration, can also be broadly divided into two  
25 parts: steps 220 to 228 which comprise the training phase of the analysis and steps 229 to 233 which comprise the prediction of the property of an unknown sample.

The training or calibration development phase consists of observing a series of blood samples 220 by diverting the samples of one or more animals of the same species through a blood loop or by otherwise observing the samples in the organisms. Additionally, for the independent quantification of property of  
30 interest, samples are obtained by withdrawing blood, step 221, from each of the animals participating in step 220.

The samples of steps 220 and 221 are analyzed on two parallel paths.

The first path consists of independent quantification of the property of interest, step 222. It is important that the independent quantification be done accurately. The accuracy of the method of the present invention  
35 is dependent upon the accuracy of the independent quantification step 222 because validation of the mathematical correlation is based on the independently quantified value of the property of interest.

The second path consists of irradiating the samples with infrared light and detecting the near infrared spectrum for each sample, step 223, and then computing all possible ratios of two wavelengths in the spectrum, step 224.

When the near infrared spectrum has been detected on a Near Infrared Systems model 6250 spectrophotometer, the near infrared spectrum from 680 to 1235 nanometers consists of 700 individual absorbance measurements. The preprocessing step of computing all possible ratios of two wavelengths expands the 700 point spectrum into 700 \* 700 or 490,000 ratio pairs. Since near infrared spectra consist of broad, slowly changing absorbance bands, computing the ratio terms using every fifth data point, 140 point  
45 spectrum, results in equivalent performance with a significant decrease in the overall computation requirement, 140 \* 140 or 19,600 ratio terms.

The preprocessed spectra for the set of training samples consisting of the calculated ratios, step 224, are correlated with the values obtained during the independent quantification step 222 by using a mathematical regression technique, step 225, such as linear regression. The pair providing the best  
50 correlation of calculated values to actual values is generally the pair of wavelengths chosen for the ratio in the mathematical correlation.

One of the outputs of this regression step is a correlation map, step 226, which graphically shows the regions of the spectrum where the most useful ratio pairs are found. The best ratio pair, step 227, is selected by identifying a region of high correlation which is also independent of small changes in the actual  
55 wavelength selected. The regression coefficients corresponding to the selected ratio pair are saved, step 228, for future application to the analysis of individual samples of unknown analyte content.

The steps 229 to 233 in FIG. 3 show the procedure to be followed for predicting hematocrit (abbreviated as HCT in FIG. 3) or hemoglobin (abbreviated as HB in FIG. 3) concentration in an individual

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unknown sample. A blood sample of unknown hematocrit or hemoglobin concentration, step 229, is observed in a dynamic condition and the near infrared spectrum of this sample is detected or measured, step 230.

5 While the near infrared spectrum of additional unknown samples may also be detected on exactly the same instrument as the training samples were measured and from which the training set spectra is prepared, it is also acceptable to use a simpler instrument which will provide the absorbance at only the two wavelengths selected to form the best ratio pair.

The ratio of the absorbance readings for the selected pair of wavelengths determined in step 227 is computed for the unknown sample, step 231. Then the regression coefficients contained in the mathematical correlation, determined during the training procedure and saved in step 228, are applied to the ratio  
10 obtained for the additional individual unknown blood sample 232, in order to yield the predicted hematocrit or hemoglobin concentration, step 233.

The ratio pre-processing technique serves to eliminate the variances of spectral data caused by scatter or other multiplicative errors in each of the various samples of both the training set and each unknown  
15 sample. This scatter would otherwise disrupt the accuracy of the detection of the training set spectra and its ability to predict the property in the unknown sample. Because both wavelengths in the selected best pair of wavelengths used in the ratio experience the same path length, variations in the effective path length due to scatter are minimized.

If the near infrared spectrum consists of N individual wavelengths, computing all possible ratios of each pair of wavelengths provides N\*N new spectral features. In FIG. 3, such computation of all possible ratios is shown at step 224. The best possible ratio pair of wavelengths must be distilled from the myriad of combinations using regression mathematical techniques, as is shown in FIG. 3, at step 225, depicted in a correlation map at step 226, and selected at step 227 for the use to determine the best possible regression coefficients in step 228 and for use with each unknown sample in step 231.  
20

Any of a number of regression techniques; such as, linear regression, multiple linear regression, stepwise regression, partial least squares regression, or principal component regression can be used to develop a statistical correlation between the ratio spectral features and the variable of the analyte being quantified. Such regression techniques are available by reference to such literature as Draper and Smith and Geladi and Kowalski publications described above for use in multiple derivative transformation. In order  
25 to determine the best ratio for a given application, regression models are computed against all possible ratio pairs of wavelengths.

Each regression model is evaluated by using an accepted statistical measure. For example, one useful measure is the simple correlation coefficient computed from the actual hematocrit value obtained from the independent quantification and the predicted hematocrit value obtained from the regression model, as is  
30 shown in FIG. 3 at step 228.

A correlation map can be constructed to visually show which wavelength ratios provide the highest correlation, as is shown in FIG. 3, at step 226. A representative correlation map for hemoglobin appears as FIG. 7. It is important to consider both high correlation and also the sensitivity of the correlation obtained to measure small changes in the actual wavelengths. The best overall ratio is found by selecting the pair of  
35 wavelengths which provide high correlation and which occur in a reasonably flat region of the correlation map.

## ANALYSIS AND VALIDATION

45

Use of the spectral analytical instrumentation described above and depicted in FIG. 1 and either of the mathematical methods described above and depicted in FIGS. 2 and 3 permit the analysis of the property of interest in the biological matter which contains water, so long as it is possible to develop a mathematical  
40 correlation between that property and water when establishing the training set through independent quantification of the property, spectra of the samples and use of the appropriate pre-processing techniques to minimize variability.

The determination of the mathematical correlation or model is founded on the linear functional relationship of the multiple linear regression equation:  $B_0 + B_1 (A_1) + B_2 (A_2) + \dots B_n (A_n) = C$  where  $B_0$  is the intercept,  $B_n$  is the regression coefficient for the nth independent variable,  $A_n$  is the nth independent variable and C is the value of the property of interest to be analyzed. Solving this equation depends upon  
45 the determination of regression coefficient(s) including the intercept and providing the values of the independent variable(s).

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When the linear functional relationship is less complex, the equation is more often expressed as the linear regression equation:  $Y = mx + b$ , where  $Y$  is the value of the property of interest to be analyzed,  $m$  is the regression coefficient indicating the slope of the line,  $b$  is the intercept of the line and  $x$  is the single independent variable. Thus, the mathematical correlation endeavors to yield a linear relationship between  
 5 the single independent variable, which is the multiple derivative transformed intensity or the ratio of the two best absorbance pairs, and the property of interest to be measured.

The linear functional relationship is more complex and involves more than one independent variable when the effect of oxygen saturation is used to adjust the mathematical correlation of hematocrit or hemoglobin concentration to the water content in whole blood. Then, the equation is expressed as a  
 10 multiple linear regression equation:  $C = B_0 + B_1 (A_1) + B_2 (A_2)$ , where  $C$  is the hematocrit or hemoglobin concentration;  $B_0$  is the intercept;  $B_1$  is the regression coefficient for the percent oxygen saturation;  $A_1$  is the percent oxygen saturation;  $B_2$  is the regression coefficient of the independent variable determined from either the multiple derivative transformation or the ratioing preprocessing.

Once the mathematical correlation is established, it is validated. The accuracy in formation and  
 15 performance is reviewed to assure reproducibility. The accuracy and precision of the mathematical correlation can be validated by physical interpretation of the selected spectral features or using additional samples analyzed by independent quantification, step 122 of FIG. 2 or step 222 of FIG. 3, and then subjecting those samples to steps 129-133 of FIG. 2 or steps 229-233 of FIG. 3, as if the samples were unknown. Statistical methods may then be used to compare the value of the predicted property, step 133 or  
 20 step 233, and the value determined by independent quantification, step 122 or step 222, to confirm reproducibility.

Standard error of calibration measures precision of formation of the model of the training set spectra, i.e., how well the regression analysis performs with the data used to construct the training set. The standard error of calibration (SEC) can be calculated from the following equation:

$$25 \quad SEC = \left[ \frac{1}{N_T - n - 1} \sum_{i=1}^{N_T} (C_i - c_i)^2 \right]^{1/2}$$

where  $N$  is the number of training samples,  $n$  is the number of absorbance terms in the regression technique employed, where  $c_i$  is the hematocrit value of the  $i$ th sample as calculated during linear  
 35 regression and  $C_i$  is the hematocrit value of the  $i$ th sample as independently determined. The smaller the SEC, the more precise the model mathematical correlation has been formed.

More importantly, the standard error of prediction (SEP) measures the assurance of reproducible performance, i.e., a test to identify quantitatively the accuracy and precision of the prediction results obtained using the method of the present invention with the actual value for the property determined by  
 40 independent quantification using known and accepted techniques and may be used in conjunction with a confidence limit to quantitatively express the accuracy of the prediction of the property being analyzed. Mathematically, the standard error of prediction can be calculated from the following equation:

$$45 \quad SEP = \left[ \frac{1}{N_p - n - 1} \sum_{i=1}^{N_p} (C_i - c_i)^2 \right]^{1/2}$$

50 where  $N$  is the number of validation samples,  $C_i$  is the independently quantified value for the  $i$ th validation sample,  $c_i$  is the value for the  $i$ th validation sample obtained using the mathematical correlation of step 131. Also, the smaller the SEP, the more accurate and precise the prediction.

Bias measures the extent of deviation of all points within a given data set in the solved mathematical equation from the line of exact correlation between predicted and actual values. Qualitatively, a low bias indicates the presence of a robustness of the training set spectra to tolerate possible error. In other words, the robustness of the training set sampling anticipates the variety of sampling possibilities for the unknown sample and minimizes its effect.  
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## INDEPENDENT VARIABLE BASED ON OXYGEN SATURATION OF HEMOGLOBIN

As stated above with reference to the flow charts depicted in FIGS. 2 and 3, the regression analysis  
5 may employ multiple variables according to the equations described above.

One multiple variable of assistance to the prediction of the property of interest is the percentage oxygen  
in the hemoglobin of whole blood, which distinguishes the hemoglobin between its oxy and deoxy forms.  
Because oxy and deoxy hemoglobin have different spectra, including in the region of 1150-1190 nm, the  
assessment of the relative contributions of both forms of hemoglobin, or a value proportional to their relative  
10 contributions, allows the adjustment of the mathematical correlation being developed for the prediction of  
hematocrit or hemoglobin concentration.

FIGS. 10 and 11 depict the schematic flow charts, similar to FIGS. 2 and 3, respectively. Reference  
numbers 320-333 in FIG. 10 depicts the same steps as reference numbers 120-133 in FIG. 2. Reference  
numbers 420-433 in FIG. 11 depicts the same steps as reference numbers 220-233 in FIG. 3. FIGS. 10 and  
15 11 add the steps in the method to adjust the mathematical correlation and the prediction to account for  
percent oxygen saturation in the whole blood. As may be seen in FIG. 10, measurement of oxygen  
saturation or a value proportional to oxygen saturation, step 334, is added to assist in performing the linear  
regression, step 325, and step 330 is modified to include the measurement of the oxygen saturation or a  
value proportional to oxygen saturation in the unknown sample. Likewise, measurement of oxygen saturation  
20 or a value proportional to oxygen saturation, step 434, is added to assist in performing the linear regression,  
step 425, and step 430 is modified to include the measurement of the oxygen saturation or a value  
proportional to oxygen saturation in the unknown sample. These alterations provide the adjustment of the  
independent variable, percent oxygen saturation or a value proportional to oxygen saturation, to the other  
independent variable, the multiple derivative transformed spectral intensity at the best wavelength or the  
25 best ratio.

The effect of percent oxygen saturation or a value proportional to oxygen saturation as an independent  
variable is linear throughout the percent oxygen saturation range. However, as percent oxygen saturation  
approaches 100 percent, the magnitude of the adjustment provided by this independent variable is  
progressively smaller, such that it becomes within the level of accuracy of the independent quantification  
30 itself.

Thus, for fully oxygenated patients, the use of the percent oxygen saturation independent variable in the  
mathematical correlation is optional. For less than fully oxygenated patients, the use of the percent oxygen  
saturation independent variable in the mathematical correlation is preferred. In emergency conditions,  
whether it is known if the patient is fully oxygenated is problematic. Therefore, for analysis of hematocrit or  
35 hemoglobin concentration, it is generally preferred to include percent oxygen saturation as an independent  
variable in the mathematical correlation.

Instruments to measure oxygen saturation of the hemoglobin concentration at the same time as the  
spectrum of whole blood is analyzed includes such commercially available instrumentation as a co-  
oximeter, a pulse oximeter, or other device which measures the oxygen saturation known to those skilled in  
40 the art. Co-oximetry typically involves measurement of oxygen saturation in a static condition. However, the  
art has progressed to measuring oxygen saturation in flowing blood such as that shown in U.S. Patent  
4,745,279.

Another method of measuring the second independent variable as a value proportional to percent  
oxygen saturation for purposes of the regression analysis depicted in FIG. 10 at 334 and 330, respectively  
45 and FIG. 11 at 434 and 430, respectively, is to employ a ratio of absorbances at two wavelengths. In other  
words, the value proportional to percent oxygen saturation is the ratio of the absorbances of two  
wavelengths where the ratio of the extinction coefficients for oxyhemoglobin and deoxyhemoglobin at one  
wavelength is different than that ratio at the second wavelength. Desirably, the ratio uses the absorbance of  
a wavelength where the extinction coefficients of oxy and deoxy hemoglobin are different, (for example at  
50 from about 680 nm to 720 nm), to the absorbance of a wavelength where the extinction coefficients of oxy  
and deoxy hemoglobins are the same, the isosbestic point. Use of the ratio of this spectral data obviates  
the need for additional oxygen saturation instrumentation.

The comparison of predicted vs. actual hematocrit or hemoglobin concentration may be graphed when  
the percent oxygen saturation is included as an independent variable. FIG. 12 shows a graph of predicted  
55 hematocrit against actual hematocrit. A comparison of FIG. 8 and FIG. 12 shows how the multiple  
independent variable mathematical correlation is generally more accurate.

Inclusion of the second variable in the regression equation serves to minimize even further any effects  
of oxygen saturation in the hemoglobin on the absorbance of the spectra at 1150-1190 nm. Thus, the

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development of a mathematical correlation which includes oxygen saturation as an independent variable enhances rather than substitutes for the method of the present invention to determine a property of interest based on its relationship to the water content in the whole blood.

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## EXTRACORPOREAL BLOOD LOOP A DYNAMIC CONDITION

An embodiment of the analysis of a property of interest in a biological fluid in a dynamic condition  
10 employs an extracorporeal blood loop. This blood loop permits "real time" monitoring of the changes in the values of the property of interest in whole blood.

When treating a patient during an operation such as open-heart surgery, a blood loop is used for oxygenation of the blood and to maintain adequate circulation. Adaptation of the equipment such as that described in FIG. 1 permits the analysis of hematocrit and hemoglobin concentration according to the  
15 methods of the present invention while the blood is moving from the body of the patient and being returned to the body of the patient. FIG. 14 identifies schematically the type of blood loop of the present invention using reference numerals while the other equipment necessary for the experiments described in the examples are identified by reference letters.

Referring to FIG. 14, the loop 500 is formed by connecting flow through cell 510 in the spectrometer S,  
20 also seen in FIG. 1 as item 113, tubing, generally 520, and valves, generally 530. The loop 500 may be separately configured to the patient P or may form a subloop to the loop already established for the patient P in the operative environment.

Loop 500 includes the following components interconnected: diversion section tubing 521 connected between the patient's blood vessel (not shown) and valve 532, diversion section tubing 522 between the  
25 valve 532 and flow through cell 510, return section tubing 523 between the flow through cell 510 and valve 534, return section tubing 524 between valves 534 and 536, return section tubing 525 between valve 536 and another blood vessel (not shown) of the patient P, and a bypass tubing section 526 between valves 532 and 536.

The tubing, generally 520, and the valves, generally 530, must be made from materials which are  
30 biocompatible with the patient's biological fluid and strong enough to withstand use of flowing pressurized fluid therethrough. A leak in the loop 500 could be traumatic for the patient P.

Preferred commercially available materials for the tubing 520 are "TYGON" brand plastic tubing available from Norton Performance Plastics of Akron, Ohio.

Preferred commercially available valves are three-way stopcock type valves marketed under the  
35 trademark "INTRALOK" from Abbott Sorenson Research of Salt Lake City, Utah.

The flow through cell 510 must be made of a transparent material used in spectrophotometric instrumentation, such as quartz plate glass, and geometrically configured and constructed in a manner to minimize the stagnation of the biological fluid in that portion of the cell irradiated with the near infrared light. Glassblowers skilled in the art are capable of configuring the cell 510, which preferably has an oval shape  
40 with opposing ports at the perimeters of sharper curvatures.

The loop 500 has a biological fluid flow in the direction of arrow F1 from the patient P through diversion section comprising tubing 521 and 522 and in the direction of arrow F2 to the patient through tubing 523, 524, and 525.

Manipulation of valves 532 and 536 allow the control of the amount of biological fluid flowing through  
45 cell 510. It is desired that adequate biological fluid flow through cell 510 during spectral detection. However, if it is desired to entirely bypass cell 510, valves 532 and 536 may be opened in a way to direct all fluid flow through section 526.

Valve 534 is adjacent the emergence of the tubing 523 from the cell 510 in order that any independent quantification needed or desired may be performed in the loop as closely as possible to the location of the  
50 spectral irradiation and detection in the cell 510.

Use of loop 500 may be combined with any spectrometric instrumentation described above, although the use of a spectrometer such as a Model 6250 spectrometer, with a computer such as a personal computer, described above is preferred.

Further, the spectra data may be gathered in conjunction with an extracorporeal blood gas sensor  
55 (EBGS) sold by Cardiovascular Devices, Inc. of Irvine, California.

Through the use of real time monitoring of the spectral data and use of the mathematical correlation obtained according to the methods of the present invention, hematocrit or hemoglobin concentration may be monitored nearly instantaneously, permitting the health care practitioner to treat the patient without delay.

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The extracorporeal loop 500 may be used in routine dialysis procedures as part of the dialysis blood loop to monitor the water content of the blood and other properties of interest. Another use of the extracorporeal loop 500 is in critical cases of prematurely born babies, neonatals, that require the use of Extracorporeal Membrane Oxygenators (ECMO) wherein a blood loop is formed with the ECMO to oxygenate the blood for days, if needed, until the proper maturation of lung functions is attained. It is a critical setting, and continuous monitoring of the blood components such as hemoglobin concentration and hematocrit among other properties, can be vital. Further, the use of loop 500 in the ECMO eliminates the undesirable need to withdraw blood samples for these analyses from the neonatal infant already in critical condition.

During the experiments recited in the examples below, it was found that approximately a 15 minute time difference exists in a mammal before any change in the concentration of oxyhemoglobin was observed after the oxygenation has been changed during the operative period. It was also noted in those experiments that approximately 3 to 4 minutes thereafter were required to complete the change of oxygenation level. Thus, nearly 20 minutes exists between the time the change in oxygenation is commenced and the oxygenation has stabilized. Current operative therapeutic monitoring involves the withdrawal of blood samples from the patient and the delivery of those samples to a remote location for static condition analysis. By the time the sample is analyzed the next stage of oxygen change may commence, thereby requiring constant withdrawal of blood samples and repeated analyses in the static condition, which delays the efforts to monitor the true hemoglobin concentration and the state of its oxygenation.

Use of a flow through cell 510 or an extracorporeal blood gas sensor with a cell 510 permits real time monitoring of the time taken to commence and complete the oxygenation change as well as maintaining in real time a monitor of the patient's condition for properties of interest such as hematocrit, hemoglobin concentration, and percent oxygen saturation.

Without being limited thereto or thereby, the following examples illustrate the methods of the present invention used to predict hematocrit and hemoglobin in whole blood in a dynamic condition using an extracorporeal blood loop.

## EXPERIMENTAL PROCEDURE FOR EXAMPLES

30

On two separate occasions, a number of whole blood spectra of canines were observed in an extracorporeal blood loop having the assembly of components depicted in FIG. 14 and described immediately above. During the course of the gathering of such spectra a number of whole blood samples were withdrawn from such canines for independent quantification of the hemoglobin concentration through the use of an "IL482" co-oximeter available from Instrumentation Laboratories or an "ABL2" blood gas analyzer available from Radiometer of Copenhagen, Denmark and independent quantification of the hematocrit by centrifuging. Also, a blank reference spectrum was obtained using an air filled cell. The diffusely transmitted light was gathered after traveling through each sample in the flow through cell 510 described above and also depicted in FIG. 1 as item 113.

All of the measurements were taken at canine body temperature, which fluctuated randomly during the spectra gathering over a range of about  $\pm$  three degrees C. or less.

Specifically, an extracorporeal blood loop was established for both of the individual sessions: the spectra set A was gathered using a 11 Kg female Beagle dog approximately two years old; and the spectra set B was gathered using a 11 Kg. female Beagle dog approximately four and one half years old. While there were some minor variations during the experimentation, the experiments used the following protocol with the following materials, instruments, and supplies.

The materials and instrumentation used for the experiment are identified by reference letters schematically in FIG. 14 and were the following:

A respirator, R, made by Bird Corporation of Palm Springs, California coupled to a semi-open anaesthesia system made by Fortec/Cyprane of Keighley, Yorkshire England connected to various pure gases such as oxygen and a mixture of 5 percent oxygen in nitrogen made by Union Carbide, Linde Division of Danbury, Connecticut sold under the trademark "MEDIBLEND™" gases;

Heated water blankets, B, "Model K20" sold by American Pharmaseal Company, American Hospital Supply Corporation, Valencia, California; "THINSULATE<sup>®</sup>" brand thermal blankets, B, made by Minnesota Mining and Manufacturing Company;

A "BURDICK" CS525 EKG-Blood Pressure Monitor, M, with a blood pressure transducer connected thereto, made by Burdick Corporation of Milton, Wisconsin;

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EKG Pregelled Electrodes #2256 made by Minnesota Mining and Manufacturing Company; cannulae, 2-1/4" long, 14 gauge made of polytetrafluoroethylene and sold under the trademark "JELCOTM" made by Jelco Labs, Rariton, New Jersey;

- Needle thermometers connected to a LED readout temperature monitor, T, available as "YSI-400" brand monitor made by Yellow Springs Instruments Company, Inc. of Yellow Springs, Ohio;
- 5 The blood loop 500 comprising "TYGON<sup>®</sup>" tubing, generally 520, having a 1.587 mm wall and a 3.175 mm internal diameter made by Norton Performance Plastics of Akron, Ohio; three-way stopcock valves, generally 530, sold under the trademark "INTRALOK<sup>®</sup>" made by Abbott Sorenson Research of Salt Lake City, Utah, a flow through cell 510 of approximately 1.6 mm path length made of quartz-plate glass made at
- 10 Minnesota Mining and Manufacturing Company for this experiment;
- A Model 6250 Pacific Scientific Infrared Spectrometer, S, having the structure described with reference to FIG. 1 and operating in wavelength ranges from 680 nm to 1235 nm;
- An IBM PS/2 Personal Computer, C, available from IBM Corporation of Boca Raton, Florida;
- A micropipette centrifuge, MC, made by Heraeus Sepatech GmbH of West Germany and distributed in the
- 15 United States by American Scientific Products of Minneapolis, Minnesota;
- An Instrumentation Laboratories "IL-482" co-oximeter, O, made by Instrumentation Laboratories of Lexington, Massachusetts;
- A "BECKMAN GPR" refrigerated centrifuge, RC, made by Beckman Instruments;
- An electro-surgical generator, ES, "Model 600" electrosurgical unit made by Minnesota Mining and
- 20 Manufacturing Company or "MODEL 9900" electrosurgical unit available from Concept Incorporated of Clearwater, Florida with a scalpel and dispersive plate system using "SCOTCHPLATE" 1145 dispersive plate and electrically conductive gel "#1103", both available from Minnesota Mining and Manufacturing Company;
- A "ABL-2" Blood Gas Analyzer, BG, made by Radiometer of Copenhagen, Denmark, represented in the
- 25 United States by Radiometer America Inc. of West Lake, Ohio; and
- A number of hand-held, test strip blood drop glucose testers commercially available under the name "GLUCOSTIX<sup>®</sup>" made by Miles Laboratories of Elkhart, Indiana.

Medical and surgical supplies used for the experiment are as follows:

- Lactated Ringers Solution, L, for injection, USP, 1,000 ml made by Abbott Laboratories, North Chicago,
- 30 Illinois;
- 0.9 percent NaCl injection, USP 1,000 ml bag, N, made by Abbott Laboratories, North Chicago, Illinois;
- "ISOFLURANE-AERRANE<sup>®</sup>" anaesthesia agent made by Anaquest of Madison, Wisconsin;
- "LYPHOMED" heparin sodium 1000 units per ml anticoagulant commercially available from Lyphomed Inc. of Rosemount, Illinois;
- 35 Acepromazine maleate commercially available under the name "ACE<sup>®</sup>, AVECOTM" from Ayerst Laboratory Inc of New York, New York in 10 mg per ml dosages;
- Atropine Sulfate Injection, 1/120 grain commercially available from Anpro Corp of Arcadia, California;
- "BIO-TAL" thiamylal sodium, USP injection available from Bioceutric Division, Boehringer Ingelheim Animal Care Inc. of St. Joseph, Missouri;
- 40 and various commonly available and used supplies such as sutures and the like.

- The method of the experiment was as follows: the Beagle dog was first administered by subcutaneous injection 0.05 mg/Kg of the sedative Acepromazine and then 0.025 mg/Kg of Atropine. Anaesthesia was induced by the administration of the barbituate Bio-tal (4%) to obtain the desired level of anaesthesia which was then sustained by the intubation of the trachea and maintained with a mixture of isoflurane in pure
- 45 oxygen from the respirator, R.

The skin was shaved on the medial aspects of the hind legs and the neck for placement of the cannulae and the animal was transferred from initial preparation areas to the operating room.

- A jugular vein cut-down at the shaved neck area was performed and the teflon cannula was inserted and connected to a drip bag containing the lactated Ringers Solution, L, dripping at the rate of 2 to 5 ml per
- 50 pound per hour. The anaesthesia was maintained by continued delivery of isoflurane at 1-2 percent delivered in pure oxygen via the semi-open anaesthesia system. Three EKG electrodes were attached on the thorax of the animal at appropriate diagnostic locations and connected via cables to the Burdick CS525 EKG-Blood Pressure Monitor, M.

- A "SCOTCHPLATE<sup>®</sup>" 1145 Electro-surgical plate (not shown in FIG. 12) was placed under the animal
- 55 on the back with an electrically conductive paste (Gel #1103 available from Minnesota Mining and Manufacturing Company) between the plate and the skin. An electro-surgical scalpel, (not shown in FIG. 12) was attached to an electro-surgical unit (ESU) generator, ES, and used to make a skin incision over the proximal medial femur with dissection carried down to expose the femoral artery and vein. Fourteen gauge



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"TEFLONTM" cannulae were inserted into the femoral artery and vein, respectively, and tied in place with a 2-0 vinyl suture. Next, the contra-lateral femoral artery similarly exposed and a 14 gauge cannulae was inserted and similarly secured with suture. This latter cannulae was connected to the Burdick Corporation blood pressure transducer, M, and connected via hydraulic lines to a pressurized bag containing 0.9 percent sodium chloride solution dripping at approximately 3 ml per hour to prevent any clogging of the cannula.

Heated water blankets, HB, with "THINSULATE<sup>®</sup>" blankets, B, were placed under and over the animal to help maintain body temperature at the initial temperature of 34.8 °C as measured by inserting the needle thermometer near the site of the contra-lateral femoral artery to indicate the core body temperature in the intestinal area. The thermometer readings were displayed on the "YSI-400" Readout Temperature Monitor, T. A second channel of that monitor was connected to a thermometer needle inserted into the tubing section 523 at the outlet port of the blood flow through cell 510 to monitor the temperature of the blood in the extracorporeal loop 500. The "TYGON<sup>®</sup>" tubing was assembled in lengths from about 30 cm to 50 cm. One stop cock valve, 532, was placed in the diversion section of the loop between tubing 521 and 522. A second stop cock valve, 536, was placed in the return section of the loop between tubing 524 and 525. Between the two valves, 532 and 536, a piece of tubing 526 was connected to provide a bypass, which by manipulation of the two valves, 532 and 536, could eliminate flow of the blood through the flow through cell 510 entirely, or to control the rate of flow therethrough.

A third stopcock valve, 534, was placed in the return section of the extracorporeal blood loop 500 between tubing 523 and 524 to permit withdrawal of samples periodically for testing of various blood related parameters using the centrifuge, MC, the co-oximeter, O, the blood gas analyzer, BG, and the glucose test strips. The flow through cell 510 was connected to the opposing ends of the diversion section at tubing 522 and the return section at tubing 523 and placed within the Model 6250 Spectrometer.

Initially the cell 510 and associated tubing 520 was filled with a 0.9% NaCl solution made by Abbott Laboratories of North Chicago, Illinois in order to remove air from the cell 510 and tubing 520 to avoid injection of air emboli upon connection of the extracorporeal loop 500 to the animal and to allow recording of a spectra of water so that known features of the water may serve as a reference of the proper functioning of the loop 500 and spectrophotometric system depicted in FIG. 1. The flow through cell 510 was approximately 6 cm long and 3.5 cm wide at the middle of the cell and mounted onto a transport metal plate of the dimensions of 11 cm by 6 cm with a circular aperture of approximately 1.5 cm. The plate was inserted into the positioning tracks of the chamber and the Model 6250 Spectrometer, S. The chamber cover was shut and taped to prevent accidental opening during the experiment.

The computer control of the cell transport mechanism was disabled by disconnecting the transport board cable between the PS/2 Personal Computer, C and the Model 6250 Spectrometer, S. This was done to prevent movement of the cell 510.

To further prevent any aberrations of the spectrometer, S, receiving incident light, the tubing 522 of the loop 500 leading to and the tubing 523 coming from the Model 6250 Spectrometer, S, was wrapped with black vinyl electrical tape available from Minnesota Mining and Manufacturing Company. Thus, the tubing itself was prevented from acting as a light guide which upon entering the cell would serve as a noise source of light.

Next, the animal was injected with 3800 units of sodium heparin from a 1,000 unit/ml solution available under the brand name "LYPHOMED". The heparin served as a blood anticoagulant because the blood in the extracorporeal loop would be in contact with various materials such as the "TEFLONTM" cannulae, valves 530, tubing 520, and the flow through cell 510.

Next the reference spectrum with air in the cell was taken and stored. Then, the loop 500 was filled with saline, making sure all trapped air bubbles were removed and then connected to patient, P.

The diversion section tubing 522 was connected to the inlet port of the cell 510 so that any spurious air bubbles would be flushed from the cell 510. Next, the extracorporeal loop 500 was adjusted at valves 532 and 536 to permit the animal's blood to flow from the animal through the flow through cell 510 and back to the animal, avoiding the bypass tubing 526 between the diversion section valve 532 and the return section 536 which would eliminate blood flow through the flow through cell 510.

After allowing the blood to flow through the cell 510 for approximately 10 minutes, a 1 ml sample of blood in a 1 ml syringe was withdrawn through valve 534 and subjected to blood gas analysis and co-oximetry and centrifuging. Less than 10 seconds after the withdrawal of the blood sample, 64 scans of spectra were acquired by the spectrometer upon initiation from the personal computer. Approximately 24 seconds were required to obtain these spectra.

Strict adherence to the protocol of blood sample handling is required to minimize aberrations. For example, blood is withdrawn into new syringes for every sample. The operation of the valve 534 where the

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blood is withdrawn must be such that only blood exiting the flow through cell 510 fills the syringe in order to avoid any blood which has proceeded further in the direction of the return to the animal has not been also withdrawn. A first one-third to one-half ml of withdrawn blood is reinjected into valve 534 positioned to direct such reinjected blood into section 524 and towards the animal. This procedure helps to force any old blood  
 5 and/or air in the valve from being also withdrawn. The next one ml of blood withdrawn in the syringe is removed for analysis by instruments, O, MC, and BG. Further, the blood from the syringe is injected into all three of the diagnostic analyzers, O, BG, and MC as soon as possible, within less than a minute, in order to obtain accurate readings not affected by atmospheric changes to the samples.

While the animal was on 100 percent inspired oxygen and confirmed by the samples analysis, the gas  
 10 was changed to a mixture of 5 percent oxygen in nitrogen. After approximately 9 minutes, another blood gas analysis was performed by withdrawal of a blood sample through valve 534 and placement in the diagnostic analytical equipment described above.

Although the percentage oxygen fell from 642 to 507 mm of Hg, the oxygen saturation of the hemoglobin was unchanged at 99.5 percent. It has been found that oxygen saturation decreases signifi-  
 15 cantly only when the percentage oxygen falls below approximately 100 mm of Hg. Because of the time delay from the change in oxygen inspiration until the oxygen saturation had stabilized, the next blood gas analysis was not taken until approximately 22 minutes. That analysis showed  $PO_2$  of 53.3 mm of Hg and  $O_2$  saturation of 93.8 percent.

Twenty-six minutes after changing the gas to 5 percent oxygen, the blood gas analysis showed an  
 20 oxygen saturation of 68.6 percent with a corresponding  $PO_2$  of 27.8 mm of Hg. Immediately after each blood gas analysis, the 64 spectra were recorded by the spectrometer, S, by initiation from the personal computer keyboard, C.

Next, using two 60 ml syringes, 100 ml of blood were withdrawn slowly from the valve 534 on the return section of the blood loop. To assure life sustaining blood pressure, the blood pressure EKG monitor, M, was  
 25 closely watched and the drip flow rate of the lactated Ringer solution, L, was increased for a few minutes to at least one drop a second to bring back or otherwise sustain blood pressure if it drops significantly from the original values recorded, 102/58 mm of Hg.

The 100 ml of blood withdrawn was centrifuged at 3000 RPM for 10 minutes in 2 centrifuge tubes of equal volumes and weights in a "BECKMAN GPR" refrigerated centrifuge, RC, utilizing a "GH-3.7" rotor  
 30 available as catalog #349702 from Beckman Instrument, Inc. of Palo Alto, California. The plasma supernatant fraction was removed with a pipette from each tube and the densely packed red blood cells in the lower portion of the centrifuge tubes were stored in the refrigerator at approximately 4° C.

The plasma was returned to the animal through the same valve 534 to maintain plasma volume but with a reduced hematocrit and hemoglobin concentration.

35 The procedure of withdrawing 100 ml of blood, centrifuging it, re-injecting the plasma and storing the red blood cells in the refrigerator was repeated several times. Each time, the blood gas analysis was performed and the spectra taken both before and after each such procedure. The hematocrit varied for each animal, e.g. for one animal from an initial percent of about 47 percent to a low of about 22 percent, at which point the refrigerated red blood cells were re-injected into the animal through the valve in the return section  
 40 of the loop to increase the hematocrit to its original level and to restore the hemoglobin concentration. Spectra were taken before and after the red blood cell re-injection into the loop and contributed to the spectra used for the training set spectra from which the mathematical regression techniques after pre-processing established the mathematical correlation between the hemoglobin concentration or hematocrit and the water content of the blood.

45

## EXAMPLES 1-6

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## SECOND DERIVATIVE PRE-PROCESSING TECHNIQUE

55

## EXAMPLE 1

The two experimental sessions were conducted according to the experimental procedure described

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above. Table I below identifies the sessions as sets A and B, and the number of samples analyzed are identified as the number of spectra obtained, which varied as shown. A representative group of samples from set A are graphed in FIG. 4. The sample spectra indicated the ranges of variability of the spectral data found, against which mathematical correlations would have been otherwise attempted to be calculated.

5 Through the use of centrifuging with centrifuge, MC, the hematocrit (Hct) found for both sets is expressed in Table I below as a range which varied from as low as 22 percent to as high as 47 percent. Similarly, the hemoglobin concentration (Hb) range in both sets was determined by cell lysing in the IL482 co-oximeter, O. The range for the sets was from about 8.0 to about 16.6 grams per deciliter (g/dL). Finally the percent oxygen saturation range (O<sub>2</sub> Sat.) in both sets was determined using the co-oximeter, O. The  
10 range for the sets was from 61 percent to 100 percent. Within each set, individual samples having oxygen saturation greater than 95 percent were segregated and assigned to a subset, A1 and B1, respectively, to distinguish the methods of the present invention between samples of nearly fully oxygenated conditions and conditions where oxygen saturation varied considerably.

15 Table I below further identifies the correlation of hematocrit to hemoglobin which demonstrated correlation for the spectra observed greater than 0.99 for both sets.

TABLE I

Sets of Samples Spectrally Analyzed and Independent Quantification Ranges of Hematocrit, Hemoglobin and Oxygen Saturation					
Set	No. of Spectra	Hct Range (%)	Hb Range (g/dL)	Hct/Hb Corr.	O <sub>2</sub> Sat. Range (%)
A	19	22-47	8.0-16.6	0.999	67.0-100.3
A1	14	22-47	8.2-10.7		99.2-100.3
B	8	24-32	8.2-10.8	0.995	61.2- 99.8
B1	6	24-31	8.0-10.7		98.5- 99.8

20 With the spectra detected, involving both the measurement of the diffuse transmission spectra and the transformation of that spectra to absorbance spectra, the analysis described in FIG. 2 and FIG. 3 was performed, using the second derivative transformation pre-processing technique and the ratio pre-processing technique, respectively, for the analysis of both hematocrit and hemoglobin.

25 While a total of 27 individual spectral detections were obtained in two sets for this example, from two individual canines, generally, it is possible to develop a training set and independent quantification training set spectral data from as few as 25 samples to as many as an infinite number of samples. When spectra in  
30 Sets A and B having greater than 95 percent oxygen saturation were segregated into Sets A1 and B1, respectively, 20 spectra were used in some of the following examples together or separately to form the training set or to validate the method. However, based on other work of some of the applicants, such as that disclosed in the European Patent Publications identified above, of the suitability of the techniques in other applications, for these purposes, the use of 20 spectra was deemed sufficient as proof of the propriety of the method of the present invention even though a more robust sampling is preferred.

35 The purpose of establishing a training set for comparisons and prediction purposes is to attempt to anticipate sampling differences which may exist in various individuals at various times. In other words, the training set should be as broad as possible to include as many variances within each of the factors affecting the measurement of the property of interest.

40 Ideally, the training set includes samples that represent all of the different kinds of changes in the hematocrit and hemoglobin concentration over a full range of values likely to be encountered in an unknown sample as well as all of the other kinds of changes within each factor likely to affect blood sampling, e.g., temperature, amount of liquids, details of light scattering, presence of other components, and physiological condition of the patient.

45 Notwithstanding such ranges of hematocrit and hemoglobin in these sets, it is seen that the correlation between hematocrit and hemoglobin is quite precise, greater over 0.99 in both sets.

50 Having established both training sets A and B and independently quantifying the hematocrit and hemoglobin ranges within each of those sets, the mathematical analysis depicted in FIG. 2 was performed.

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First, the second derivative pre-processing technique was performed against the combination of the sets using the Near Infrared Spectral Analysis software program described above, with a personal computer described above, and available with the Model 6250 spectrometer from Near Infrared Systems to compute the second derivatives, to perform the linear regression, to select the best wavelength, and to save the regression coefficients (steps 124, 125, 127, 128, and 131 of FIG. 2). Other software, "VAX IDL Interactive Data Language" available from Research Systems, Inc. (copyright 1982-1988) was used to apply the regression model, predict the property, (steps 132 and 133 of FIG. 2) and to compute the SEC, SEP, and the bias for validation purposes. In these Examples the approximated second derivative spectra obtained was based on the use of segment of 20 datapoints or 15.8 nm and a gap of 0 datapoints. Thus, each point for purposes of calculating the second derivative was a band 15.8 nm wide without any gap between the bands.

The group of spectra for Set A are shown in FIG. 4 are re-depicted in FIG. 5 after the second derivative pre-processing has been performed. As may be readily seen, the variations in absorbances as caused by baseline offsets and other variances from spectrum to spectrum are minimized, permitting better attempted mathematical correlation.

The second derivative pre-processing technique computes a transformed absorbance value for all of the wavelengths in order to find the best correlation in the area of the water absorbance peak.

For the analysis of hemoglobin, Sets A and B were combined, comprising 27 spectra. Using second derivative transformation as the pre-processing technique, the mathematical analysis depicted in FIG. 2 was performed and yielded a wavelength of 892 nm with a multiple correlation coefficient (R) of 0.991 and a standard error of calibration (SEC) of 0.39 g/dL. However, this wavelength is within a region of the spectrum where a broad absorbance peak of hemoglobin exists and which peak is dependent upon on the percent oxygen saturation. Further use of a wavelength chosen from a set of spectra which is near the minimum number of spectra desired for a versatile training set can be rejected because the smaller training set can invert the priority of correlation of the various wavelengths to the actual value determined by independent quantification.

Another reason for rejection of a wavelength in the 900 nm region of broad hemoglobin absorbance is the possible interference by other forms of hemoglobin absorbing in this region, such as methemoglobin.

Therefore, to find a wavelength which did not exist in a region substantially affected by the spectra of the various forms of hemoglobin, a correlation plot was generated, using the Near Infrared Spectral Analysis software described above or the "VAX IDL, Interactive Data Language" described above. FIG. 6 depicts that correlation plot. As seen in FIG. 6, the correlation in the region of 890 nm is an anomalously sharp band where variations in the wavelength selected can significantly reduce the extent of correlation. Conversely, the correlation in the region of 1150 to 1190 nm is a broader band where variations in the wavelength selected do not significantly reduce the extent of correlation. As discussed below, predictions using a wavelength within this range are acceptable.

From that plot, it was found that in the range of 1150 to 1190 nm corresponding to the broad absorbance peak of the water content, use of a wavelength within the range of 1160-1175 nm, specifically, 1170 nm, had acceptable correlation for generating a calibration equation. The results of the mathematical analysis computed from using the Near Infrared Spectral Analysis software described above and the VAX IDL software described above in the same manner as described earlier in this Example using 1170 nm yielded a R = 0.9064, and SEC = 1.20 g/dL. The slope was 126.3, and the intercept was 3.132. Thus, in this instance, the linear functional equation using a single independent variable was:

$$\text{Concentration of Hemoglobin} = 3.13 + 126.32 * (\text{Second Derivative of Spectral Intensity at Wavelength } 1170 \text{ nm})$$

By choosing to concentrate on the water absorbance peak around 1150 to 1190 nm, and particularly around 1160 to 1175 nm where there is far less absorbance of either form of hemoglobin than in the region of 925 nm, the mathematical correlations achieved were deemed more acceptable because the correlation was more resistant to errors caused by variations in percent oxygen saturation, and as seen below, SEP and bias were acceptable. Thus, applying the multiple derivative transformation pre-processing technique, variability is minimized when using a wavelength corresponding to the absorbance of the water content in whole blood.

## EXAMPLE 2

To validate the performance of the correlation model at about 1170 nm, the combined sets A + B were

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then used as a known set to predict sets A, A1, B and B1, as if such were unknown. The Near Infrared Spectral Analysis software was used to generate the model combining Sets A and B, and the VAX IDL software was used to compute the results. Table II shows the results found.

TABLE II

Prediction of Individual Sets Against Combined Set A + B For Hemoglobin at 1170 nm After Second Derivative Pre-Processing			
Set	R	SEC g/dL	Bias g/dL
A1	0.995	0.84	0.56
A	0.930	1.13	0.03
B1	0.993	0.72	0.57
B	0.456	1.31	-0.07

The distinctions between the prediction of sets A and B compared with sets A1 and B1 were multiple. The prediction performed well using sets A1 and B1 when the percent oxygen saturation was measured as greater than 95 percent. Correlation R was more precise with the segregated sets A1 and B1, and SEC's were less than 1.0 g/dL. However, the five spectra of set A not found in set A1 and the two spectra of set B not found in set B1 lowered the R and raised the SEC, indicating a less precise prediction achieved. Further, the bias trended more negatively as the lower percent oxygen saturation spectra were included in the set predicted, indicating the lower percent oxygen saturation spectra individually were predicted consistently lower than the higher percent oxygen saturation spectra.

While the use of the second derivative pre-processing technique at the spectral intensity of around 1170 nm wavelength is acceptable for certain instances in a dynamic condition, the acceptability is more apparent under conditions where the percent oxygen saturation is greater than 95 percent.

**EXAMPLE 3**

The validation of the performance of the selected linear functional equation described in Example 1 was performed to assess standard error of prediction (SEP) and bias. Each set was used as a known and used to predict each other set as if such other set were unknown. The Near Infrared Spectral Analysis software and the VAX IDL software were used in the same manner as described in Example 1 and used in Example 2 to compute the results. Table III shows the results found.

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TABLE III

Prediction of Individual Sets Against Other Individual Sets For Hemoglobin at 1170 nm After Second Derivative Pre-Processing							
Known Set	R	SEC g/dL	Slope	Intercept	Unknown Set	SEP g/dL	Bias g/dL
A1	0.995	0.29	155.7	0.35	B1	0.64	-0.50
A	0.922	1.18	136.2	2.39	B	2.06	-1.24
B1	0.992	0.16	142.5	1.63	B1	0.50	0.39
B	0.406	1.05	43.5	7.48	B	1.40	-0.29
					A1	0.47	0.20
					A	1.18	-0.35
					A1	2.31	-1.13
					A	2.62	-1.49

The same trends found in Table II were more accentuated in the results shown in Table III. The prediction using one segregated set A1 against another, B1, and vice versa demonstrated the precision of the linear functional equation within an acceptable range. The prediction using full set A against full set B, and vice versa, was less acceptable without possible further adjustment using another independent variable such as percent oxygen saturation. The prediction of a segregated set against a full set, e.g., using A1 to predict B, compared with using a full set to predict a segregated set, e.g., using A to predict B1, demonstrated the desirability of having a broadly based known training set. The breadth of the training set must be adequately balanced among spectra of various types. Only two spectra of eight spectra in set A were not present in set B1. Yet those two spectra were so different due to percent oxygen saturation as to effect greatly the R, SEC, SEP, and bias. However, the five of nineteen spectra missing from set A in set A1 did not cause comparable lack of prediction precision. Therefore, planning great variations in the construction of the training set with balance among the variations will provide the better results for precise prediction.

The bias results in Table III demonstrated accuracy of the linear functional equation, when considering known sets A1, B1 and A. Yet the trend in each instance of prediction where the unknown set included spectra having lower percent oxygen saturation was more negative, indicating an under-prediction of the property of interest.

## EXAMPLE 4

The same experiments as those described in Examples 1-3 were conducted for the analysis of hematocrit using the second derivative transformation pre-processing technique computed using the Near Infrared Spectral Analysis software and the VAX IDL software in the same manner as described in Examples 1-3. The combined sets A and B were analyzed for the best wavelength not likely to be rendered inaccurate by changes in concentration of the various forms of hemoglobin, i.e., in the range of 1150-1190 nm. The combined sets having 27 individual spectra, yielded acceptable results.

As in the case of the hemoglobin of Example 1, the wavelength initially selected by the mathematical analysis was around 892 nm, (R = 0.987 and SEC = 1.28%) in the region of a broad hemoglobin absorbance peak. Therefore, using a correlation plot generated in the same manner as that for Example 1, it was determined that use of a wavelength in the region of 1150-1190 would provide acceptable results. The wavelength between 1160 and 1175 nm was chosen, 1169 nm, and provided the following results: R = 0.899 and SEC = 3.47% with a slope of 356.17 and an intercept of 10.19.

The combined set A + B was then used as a known set and the individual sets A1, A, B1, and B were predicted therefrom to assess standard error of calibration. The results are shown in Table IV.

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Table IV

Predict Individual Sets Against the Combined Set For Hematocrit at 1169 nm After Second Derivative Pre-Processing			
Set	R	SEC (%)	Bias (%)
A1	0.996	2.56	1.75
A	0.934	3.21	0.27
B1	0.984	1.77	1.29
B	0.404	3.99	-0.64

As seen in Table IV, sets A1 and B1 were more precise than sets A and B. The change in bias from smaller sets A1 and B1 to sets A and B, respectively, was more negative, again indicating the trend in accuracy of the linear functional equation to under-predict spectra having lower percent oxygen saturation.

The individual sets A1, A, B1, and B were treated as known sets and the other sets were treated as unknown sets to assess standard error of prediction and bias. Table V shows the results obtained.

TABLE V

Predict Individual Sets Against Other Individual Sets For Hematocrit at 1169 nm After Second Derivative Pre-Processing							
Known Set	R	SEC (%)	Slope	Intercept	Unknown Set	SEP (%)	Bias (%)
A1	0.996	0.73	450.0	1.71	B1	2.54	-1.99
A	0.926	3.29	395.3	7.22	B	6.62	-4.21
B1	0.956	0.63	420.1	5.54	B1	0.89	0.47
B	0.362	3.21	117.0	22.43	B	4.52	-1.58
					A1	1.79	1.38
					A	3.14	-0.21
					A1	6.42	-2.54
					A	7.22	-3.52

As seen in comparison with the results shown in Table III, the same or similar trends were found for hematocrit as found for hemoglobin concentration. Segregated sets A1 and B1 provided the more precise predictions, but the larger set A having a better balance of percent oxygen saturation spectra variations predicted set B1 with acceptable precision. The prediction by set B and the prediction of set B showed the effects that two outlier spectra can have on a smaller set having less robustness of spectra.

Bias for the predictions by all of the sets were more positive when predicting the segregated sets A1 or B1 than when predicting the full sets A or B, again indicating an under-prediction is possible when the spectra has a lower percent oxygen saturation.

FIG. 8 is a graph of the comparison of predictions of set A to the actual independently quantified values for hematocrit.

## EXAMPLE 5

Thus, it was determined that in the dynamic condition of whole animal blood, better results were obtained consistently when the model was confined to occasions when the samples being analyzed had

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greater than about 95 percent oxygen saturation. While that condition exists in the great majority of patient diagnostic circumstances, there are many occasions when the patient may have less than 95 percent oxygen saturation. For humans, that is known to be in circumstances when the partial pressure of oxygen in the patient is less than about 60 mm of Hg.

Therefore, as an optional methodology, the percent oxygen saturation of the patient was added as an independent variable to the linear functional equation and multiple linear regression analysis or the like was performed as depicted in FIG. 10 in the case of multiple derivative transformation pre-processing. With two animals studied, the percent oxygen saturation was measured for each spectrum using the "IL-482" co-oximeter. That data comprised one column of data used in replacement of one column of spectral data to achieve a multiple variable set of data, which the Near Infrared Spectral Analysis software and the VAX IDL software computed in the manner described in Examples 1-3 to yield the mathematical results.

Table VI shows the results found when individual sets were used to predict other individual sets for hemoglobin where the percent oxygen saturation was added to the mathematical analysis as an independent variable. Table VII shows the analogous results for hematocrit.

TABLE VI

Prediction of Individual Sets Against Other Individual Sets With Adjustment For Percent Oxygen Saturation From A Co-Oximeter For Hemoglobin at 1170 nm After Second Derivative Pre-Processing								
Known Set	R	SEC g/dL	O <sub>2</sub> Slope	Slope	Intercept	Unknown Set	SEP g/dL	Bias g/dL
A	0.996	0.27	-0.109	159.01	11.00	B1	0.76	-0.51
B	0.999	0.16	-0.083	147.63	9.59	B	0.62	-0.32
						A1	0.49	0.28
						A	0.46	0.15

TABLE VII

Prediction of Individual Sets Against Other Individual Sets With Adjustment For Percent Oxygen Saturation From A Co-Oximeter For Hematocrit at 1169 nm After Second Derivative Pre-Processing								
Known Set	R	SEC %	O <sub>2</sub> Slope	Slope	Intercept	Unknown Set	SEP %	Bias %
A	0.997	0.70	-0.305	459.66	31.50	B1	2.97	-2.01
B	0.983	0.69	-0.253	439.55	29.64	B	2.36	-1.62
						A1	2.08	1.68
						A	1.78	1.38

With the use of the complete sets A or B as the known set, a direct comparison was made between the results shown in Tables III and VI and V and VII, respectively. In every instance other than the already acceptable prediction by set A of set B1, use of percent oxygen saturation as a second independent variable provided a higher correlation R, a more precise SEC, a more accurate and precise SEP, and a more accurate bias. Also, the under-prediction reflected in the change in bias between prediction of segregated sets B1 or A1 and full sets B or A was less pronounced.

The greatest adjustment provided by including the percent oxygen saturation as an independent variable occurred with respect to set 9, previously seen as extremely marginal in prediction as either the known set or the unknown set. Thus, the percent oxygen saturation contributes more to the accuracy and precision of the prediction when the percent oxygen saturations for the spectra are more varied.

For a known occasion where percent oxygen saturation is lower than 95 percent or for an unknown occasion, use of a linear functional equation including percent oxygen saturation as a second independent



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variable provided most useful results. FIG. 12 shows the high resolution of accuracy between the method used in this Example 5 and the independent quantification used for the same spectra and how that resolution is more accurate than that shown in FIG. 8.

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**EXAMPLE 6**

The effect of variations in percent oxygen saturation among the spectra was also calculated from the spectra without use of the co-oximeter. The ratio of the wavelengths of 700 and 820 nm, was proportional to the percent oxygen saturation which existed in each sample as it was analyzed. That ratio data from the originally detected spectra replaced one column of transformed spectral data to achieve a multiple variable set of data, which the Near Infrared Spectral Analysis software and the VAX IDL software computed in the manner described in Examples 1-3 to yield the mathematical results. Table VIII shows the results found for hemoglobin when the adjustment for percent oxygen saturation was determined by the ratio described here. Table IX shows the analogous results found for hematocrit.

**TABLE VIII**

Prediction of Individual Sets Against Other Individual Sets With Adjustment For Percent Oxygen Saturation From A Spectral Ratio For Hemoglobin at 1170 nm After Second Derivative Pre-Processing								
Known Set	R	SEC g/dL	O <sub>2</sub> Slope	Slope	Intercept	Unknown Set	SEP g/dL	Bias g/dL
A	0.997	0.259	13.07	168.9	-11.33	B1	0.94	-0.52
						B	0.73	-0.46
B	0.981	0.242	11.84	166.4	-9.624	A1	0.62	0.48
						A	0.59	0.48

**TABLE IX**

Prediction of Individual Sets Against Other Individual Sets With Adjustment For Percent Oxygen Saturation From A Spectral Ratio For Hemoglobin at 1170 nm After Second Derivative Pre-Processing								
Known Set	R	SEC %	O <sub>2</sub> Slope	Slope	Intercept	Unknown Set	SEP %	Bias %
A	0.997	0.72	36.46	495.38	-31.18	B1	3.90	-2.19
						B	2.67	-2.18
B	0.970	0.92	36.05	496.69	-28.69	A1	2.72	2.22
						A	2.61	2.22

A comparison of the results shown in Table VIII with Table VI and shown in Table IX with Table VII found that the use of a ratio of wavelengths from the same spectral data as that used in the prediction found the accuracy and precision of the prediction to be comparable.

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**EXAMPLES 7-10****RATIO PRE-PROCESSING TECHNIQUE**

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## EXAMPLE 7

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The use of a ratio pre-processing technique provided comparable results to the use of the multiple derivative pre-processing technique. Using the same spectra and data as shown in Table I in Example I, the ratio pre-processing method depicted in FIG. 3 was employed using the following Fortran generated software program described herein, with a personal computer, to select the best ratio, to perform the linear regression, and to save the regression coefficients (steps 224, 225, 227, and 228 of FIG. 3). Procedures in the VAX IDL Interactive Data Language software program described in Example 1 were used to perform the ratio pre-processing on the unknown sample, apply the regression model and predict the property, (steps 231, 232, and 233 of FIG. 3) and to compute the SEC, SEP, and bias for validation purposes.

15

Fortran Software Program (Complies with ANSI  
Fortran 77) Copyright, 1989, Minnesota Mining and  
Manufacturing Company

20

```
REAL DATA(200,500),YVAL(200),TEMP(1500)
```

```
REAL DOUT(500,500),NSPEC,NWAVE
```

```
CHARACTER*30 FILEN
```

25

```
WRITE (6, 100)
```

```
100 FORMAT ( ' ENTER THE SPECTRAL DATA FILE NAME: ' )
```

```
READ (5, 101) FILEN
```

```
101 FORMAT (A)
```

30

```
OPEN (20, FILE=FILEN, STATUS='OLD',
```

```
1FORM='UNFORMATTED', ERR=9999)
```

```
READ (20) NSPEC, NWAVE
```

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```

10 WRITE (6,102)
5 102 FORMAT ( ' ENTER SPACING BETWEEN SPECTRAL POINTS: ' )
    READ (5,*) NSKIP
    IF (NWAVE/NSKIP .GT. 500) GOTO 10
    DO 20 I=1,NSPEC
10    READ (20) (TEMP(J), J=1, NWAVE)
    DO 20 J=0,NWAVE/NSKIP-1
20    DATA(I,J+1) = TEMP(NSKIP*J+1)
    CLOSE (20)
15    WRITE (6, 103)
103 FORMAT ( ' ENTER THE PROPERTY DATA FILE NAME: ' )
    READ (5, 101) FILEN
20    OPEN (20, FILE=FILEN, STATUS='OLD',
    1FORM='UNFORMATTED', ERR=9999)
    READ (20) NSPEC
    DO 30 I=1,NSPEC
25    30 READ (20) YVAL(I)
    CLOSE (20)
    AVEY = YVAL(1)
30    DO 40 I=2,NSPEC
40    AVEY = AVEY + YVAL(I)
    AVEY = AVEY / NSPEC
    YFACT = 0.0
35    DO 50 I = 1, NSPEC
50    YFACT = YFACT + (YVAL(I)-AVEY)*(YVAL(I)-AVEY)
    IF (YFACT .LT. 1.0E-06) GO TO 9999
40    ZCORR = 0.0
    DO 80 I=1,NWAVE/NSKIP
    DO 80 J=1,NWAVE/NSKIP
    AVEX=0.0
45    DO 60 K=1,NSPEC
    TEMP(K) = DATA(K,J)/(DATA(K,I)+1.0E-6)
60    AVEX = AVEX + TEMP(K)
    AVEX = AVEX / NSPEC
50    XFACT = 0.0
    XYFACT = 0.0
    DO 70 K=1,NSPEC
55    XFACT = XFACT + (TEMP(K)-AVEX)*(TEMP(K)-AVEX)

```

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```

70 XYFACT = XYFACT + (TEMP(K)-AVEX)*(YVAL(K)-AVEY)
  IF (ABS(XFACT) .LT. 1E-6) DOUT(J,I)=0.0
  IF (ABS(XFACT) .GE. 1E-6)
1DOUT(J,I)=(XYFACT/XFACT)*(XYFACT/YFACT)
  IF (DOUT(J,I) .LE. ZCORR) GO TO 80
10 ZCORR = DOUT(J,I)
  ZXCOL = J
  ZYCOL = I
  ZAVEX = AVEX
15 ZXFACT = XFACT
  ZXY = XYFACT
80 CONTINUE
20 WRITE (6,104) INT(1+(ZXCOL-1)*NSKIP),
  INT(1+(ZYCOL-1)*NSKIP)
104 FORMAT (/, ' NUMERATOR WAVELENGTH: ', I4,
25 1/, ' DENOMINATOR WAVELENGTH: ', I4)
  SLOPE = ZXY/ZXFACT
  WRITE (6,105) ZCORR, SLOPE, AVEY-SLOPE*ZAVEX
105 FORMAT (/, ' CORRELATION COEFF.: ', 1PE11.4,
30 1/, ' SLOPE: ', E10.3,/, ' INTERCEPT: ', E10.3)
  WRITE (6,106)
106 FORMAT ( ' ENTER THE OUTPUT FILE NAME: ' )
  READ (5, 101) FILEN
35 OPEN (20, FILE=FILEN, FORM='UNFORMATTED',
  STATUS='NEW')
  WRITE (20) NWAVE/NSKIP,NWAVE/NSKIP,0.0,0.0
40 DO 90 I=1,NWAVE/NSKIP
  90 WRITE (20) (DOUT(J,I), J=1,NWAVE/NSKIP)
9999 CLOSE (20)
  STOP
45 END

```

The ratio pre-processing technique computed substantially possible wavelength pairs, as described above, in order to find the best correlation in the area of the water absorbance peak and another absorbance measuring point.

For the analysis of hemoglobin, Sets A and 8 were combined, comprising 27 spectra. Using the ratio pre-processing technique, the mathematical analysis depicted in FIG. 3 was performed and yielded a pair of wavelengths of 843 and 1173 nm with a multiple correlation coefficient (R) of 0.996 and a standard error of calibration (SEC) of 0.26 g/dL, with a computed slope of 36.818 and an intercept of -37.807. This pair is in the vicinity of the isosbestic point for oxy and deoxy hemoglobin and the broad absorbance peak of water, respectively. However, for purposes of comparison with the examples of ratio pre-processing technique used in U.S. Patent Application Serial Number 07/408,746, filed by some of the applicants of this application, the pair of wavelengths of 820 and 1161 nm were chosen, which yielded the nearly similar

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results of  $R = 0.983$ ,  $SEC = 0.53$  g/dL, and a slope of 40.347 and intercept of -40.773.

To confirm the selection of the 820/1161 pair of wavelengths, a correlation map was generated, and depicted as FIG. 7 using the VAX IDL, Interactive Data Language software described above.

From that map measuring the lines of equal correlation at 0.875, 0.90, 0.925, 0.95, and 0.975 using the squares of the multiple correlation coefficients, it was found that in the range of 1150 to 1190 nm corresponding to the broad absorbance peak of the water content had a broad plateau. The range of 800 to 850 nm also showed a broad plateau. Pairs of wavelengths within these regions would provide acceptable results.

Thus, in this instance using procedures in the VAX IDL software described above and the ratio of 820 nm to 1161 nm, the linear functional equation using a single independent variable was:  
Hemoglobin  $-40.773 + 40.347 * (\text{Absorbance}_{820} / \text{Absorbance}_{1161})$

Table X shows the results found using this equation as applied to predict each set A1, A, B1, and B against the combined set A + B for hemoglobin concentration.

TABLE X

Prediction of Individual Sets Against Combined Set For Hemoglobin at Ratio of 820/1161 nm			
Set	R	SEC g/dL	Bias g/dL
A1	0.998	0.32	-0.16
A	0.992	0.39	0.00
B1	0.994	0.36	-0.22
B	0.832	0.92	0.14

A comparison of the results found in Table X with the results found in Table II showed the relatively more precise linear functional correlation using the ratio pre-processing technique. However, among the sets studied in Table X, set B showed the effects on precision of lower percent oxygen saturation spectra creating an imbalance within a set of limited numbers for the training set. With adequate balance of variations in the training set spectra, even if the unknown sample's spectrum were quite abnormal, use of ratio pre-processing technique in the formation of the linear functional correlation would have provided acceptable results for calibration.

The validation of the performance of the selected linear functional equation described in this Example 7 was performed to assess standard error of prediction (SEP) and bias. Each set was used as a known and used to predict each other set as if such other set were unknown. Table XI shows the results found.

TABLE XI

Prediction of Individual Sets Against Other Individual Sets For Hemoglobin After Ratio Pre-Processing at 820/1161 nm							
Known Set	R	SEC g/dL	Slope	Intercept	Unknown Set	SEP g/dL	Bias g/dL
A1	0.998	0.20	42.817	-43.793	B1	0.34	-0.21
					B	0.99	0.18
A	0.992	0.39	41.071	-43.683	B1	0.42	-0.27
					B	0.93	0.10
B1	0.995	0.15	43.195	-44.047	A1	0.34	0.24
					A	0.63	0.42
B	0.832	0.70	26.227	-23.170	A1	1.63	-0.99
					A	1.59	-0.98

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The results provide proof of the accuracy and the precision of the linear functional equation for predicting hemoglobin in a dynamic condition of an extracorporeal blood loop of a mammal. Recognizing the effects of outlier spectra in set B as previously described in a smaller set than that to be used in forming the training set, the most precise predictions arise from segregated sets A1 and B1, followed by the predictions of and with set A. The trend in the bias is slightly toward the positive, but all sets were predicting within a range of acceptable bias.

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## EXAMPLE 8

The same experiments as those described in Example 7 were conducted for the analysis of hematocrit using the ratio pre-processing technique computed using the same software and procedures as described in Example 7. The combined sets A and B were analyzed for the best wavelength pair not likely to be rendered inaccurate by changes in concentration of the various forms of hemoglobin, i.e., in the range of 1150-1190 nm and around the isosbestic point. The combined sets having 27 individual spectra, yielded acceptable results.

As in the case of the hemoglobin of Example 7, the wavelength pair initially selected by the mathematical analysis was around 855 nm and 1161 nm ( $R = 0.993$  and  $SEC = 0.93\%$ ) with the former in the region of a broad hemoglobin absorbance peak. Therefore, using a correlation map generated in the same manner as that for Example 7, it was determined that use of the same wavelength pair of 820/1161 nm would provide acceptable results. That wavelength pair yielded the following results:  $R = 0.982$  and  $SEC = 1.54\%$ , with a slope of 112.74 and an intercept of -113.62.

The combined set A + B was then used as a known set and the individual sets A1, A, B1, and B were predicted therefrom to assess standard error of calibration. The results are shown in Table IV.

TABLE XII

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Predict Individual Sets Against The Combined Set For Hematocrit After Ratio Pre-Processing at 820/1161 nm			
Set	R	SEC (%)	Bias (%)
A1	0.998	0.93	-0.29
A	0.991	1.25	0.15
B1	0.987	1.94	-1.25
B	0.835	2.52	-0.35

As seen in Table XII, sets A1 and B1 were more precise than sets A and B. The change in bias from smaller sets A1 and B1 to sets A and B, respectively, was more positive. But all were within acceptable ranges.

The individual sets A1, A, B1, and B were treated as known sets and the other sets were treated as unknown sets to assess standard error of prediction and bias. Table XIII shows the results obtained.

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TABLE XIII

Predict Individual Sets Against Other Individual Sets For Hematocrit After Ratio Pre-Processing at 820/1161 nm							
Known Set	R	SEC (%)	Slope	Intercept	Unknown Set	SEP (%)	Bias (%)
A1	0.998	0.53	122.53	-126.08	B1	2.32	-1.57
A	0.991	1.18	117.50	-120.02	B	2.80	-0.53
					B1	2.58	-1.75
B1	0.987	0.68	125.02	-127.60	B	2.87	-0.78
					A1	2.03	1.73
B	0.835	2.08	78.72	-70.63	A	2.82	2.29
					A1	3.63	-1.61
					A	3.57	-1.52

As seen in comparison with the results shown in Table XI, the same or similar trends were found for hematocrit as found for hemoglobin concentration. Segregated sets A1 and B1 provided the more precise predictions against each other, but the larger sets A and B have acceptable precision. The prediction by set B and the prediction of set B showed the effects that two outlier spectra can have on a smaller set having less robustness of spectra, although the effect is less pronounced using the ratio pre-processing technique compared with the second derivative transformation pre-processing technique.

Bias for the predictions by all of the sets were more negative when predicting the segregated sets A1 or B1 than when predicting the full sets A or B, indicating a possible over-prediction is possible when the spectra has a lower percent oxygen saturation. But the bias in all sets' predictions is acceptable.

FIG. 9 is a graph of the comparison of predictions of set A to the actual independently quantified values for hematocrit.

## EXAMPLE 9

As counterpoint to the experiments of Example 5, the use of the percent oxygen saturation was employed as a second independent variable while using the ratio pre-processing technique even though consistently acceptable results were obtained with a single independent variable linear functional equation. FIG. 11 depicts the method of the invention altered to adjust for the use of the second independent variable. The 820/1161 nm ratio computed with the VAX IDL software was added with the co-oximeter measurements to produce a linear summation, and then computed with a multiple linear regression analysis procedure of the VAX IDL software to yield the mathematical results. Tables XIV and XV show the results found when including the co-oximeter measurements of percent oxygen saturation into the equation for hemoglobin and hematocrit, respectively.

TABLE XIV

Prediction of Individual Sets Against Other Individual Sets With Adjustment For Percent Oxygen Saturation From A Co-Oximeter For Hemoglobin After Pre-Processing at 820/1161 nm								
Known Set	R	SEC g/dL	O <sub>2</sub> Slope	Slope	Intercept	Unknown Set	SEP g/dL	Bias g/dL
A	0.997	0.23	0.0273	41.506	-44.820	B1	0.33	-0.15
B	0.945	0.46	0.0418	41.935	-46.633	B	0.56	-0.03
						A1	0.30	0.17
						A	0.32	0.11

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TABLE XV

Prediction of Individual Sets Against Other Individual Sets With Adjustment For Percent Oxygen Saturation From A Co-Oximeter For Hematocrit After Ratio Pre-Processing at 820/1161 nm								
Known Set	R	SEC %	O <sub>2</sub> Slope	Slope	Intercept	Unknown Set	SEP %	Bias %
A	0.997	0.67	0.0850	118.86	-129.79	B1	2.55	-1.38
B	0.928	1.58	0.1129	121.17	-134.02	B	2.36	-1.18
						A1	1.91	1.54
						B	1.77	1.42

With the use of the complete sets A and B as the known set, a direct comparison was made between the results shown in Tables XI and XIV and XIII and XV, respectively. In every instance, use of percent oxygen saturation as a second independent variable provided a higher correlation R, a more precise SEC, a more accurate and precise SEP, and a smaller bias, than the already acceptable results using the linear functional equation with the single ratio pair independent variable. While there was less adjustment for set B than found to be necessary in Examples 1-6, there was more adjustment provided by the second independent variable for set 8 than for the other sets. Thus, the percent oxygen saturation contributes more to the accuracy and precision of the prediction when the percent oxygen saturations for the spectra are more varied.

For a known occasion where percent oxygen saturation is lower than 95 percent or for an unknown occasion, use of a linear functional equation including percent oxygen saturation as a second independent variable provided most useful results. FIG. 13 shows the high resolution of accuracy between the method used in this Example 9 and the independent quantification used for the same spectra and how that resolution is more accurate than that shown in FIG. 9.

## EXAMPLE 10

The effect of variations in percent oxygen saturation among the spectra was also calculated from the spectra without use of the co-oximeter. The ratio of the absorbances at the wavelengths of 700 and 820 nm was proportional to the percent oxygen saturation existing in each sample as it was analyzed. The 820/1161 nm ratio computed with the VAX IDL software was added with the 700/820 nm ratio to produce a linear summation, and then computed with a multiple linear regression analysis procedure of the VAX IDL software to yield the mathematical results. Table XVI shows the results found for hemoglobin when the adjustment for percent oxygen saturation was determined by the ratio described here. Table XVII shows the analogous results found for hematocrit.



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TABLE XVI

Prediction of Individual Sets Against Other Individual Sets With Adjustment For Percent Oxygen Saturation From A Spectral Ratio For Hemoglobin After Ratio Pre-Processing at 820/1161 nm								
Known Set	R	SEC %	O <sub>2</sub> Slope	Slope	Intercept	Unknown Set	SEP %	Bias %
A	0.998	0.21	-3.109	40.758	-38.561	B1	0.35	-0.17
B	0.960	0.39	-5.421	40.725	-36.410	B	0.56	-0.02
						A1	0.36	0.24
						A	0.35	0.12

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TABLE XVII

Prediction of Individual Sets Against Other Individual Sets With Adjustment For Percent Oxygen Saturation From A Spectral Ratio For Hematocrit After Ratio Pre-Processing at 820/1161 nm								
Known Set	R	SEC %	O <sub>2</sub> Slope	Slope	Intercept	Unknown Set	SEP %	Bias %
A	0.998	0.60	-9.647	116.54	-110.40	B1	2.61	-1.43
B	0.943	1.40	-14.858	118.46	-106.91	B	2.30	-1.14
						A1	2.18	1.77
						A	1.88	1.49

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A comparison of the results shown in Table XVI with Table XIV and shown in Table XVII with Table XV found that the use of a ratio of wavelengths from the same spectral data as that used in the prediction were quite comparable and acceptable.

Embodiments of the invention have been described using examples. However, it will be recognized that the scope of the invention is not to be limited thereto or thereby.

### Claims

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1. A method for analyzing a property of biological matter having a water content in a dynamic condition, the biological matter comprising a first compartment related to the property to be analyzed and a second compartment having a proportionally larger or smaller amount of water than the first compartment, the method comprising:

- 45 (a) observing multiple samples of biological matter in a dynamic condition;  
 (b) irradiating with near infrared light said multiple samples of the biological matter;  
 (c) detecting the near infrared absorption spectrum of each of said multiple samples;  
 (d) applying a ratio pre-processing technique to the absorption spectrum of each of said multiple samples;  
 (e) independently quantifying the property to be analyzed for each of said multiple samples;  
 50 (f) establishing a training set from said near infrared absorption spectra of said multiple samples; and  
 (g) statistically identifying the nature of a mathematical correlation between the property to be analyzed in the first compartment and the water content in the biological matter;  
 wherein said ratio pre-processing technique comprises applying a ratio of a near-infrared wavelength absorbance peak of the water content in said training set to another near-infrared wavelength absorbance  
 55 measuring point in said training set.

2. A method according to Claim 1, further comprising the steps of:  
 (h) observing an unknown sample of the biological matter in a dynamic conditioning;  
 (i) irradiating said unknown sample of the biological matter with near infrared light;

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- (j) detecting the near infrared spectrum of said unknown sample;  
 (k) applying said ratio pre-processing technique to said spectrum of said unknown sample; and  
 (l) predicting the property to be analyzed in said unknown sample by utilizing said mathematical correlation obtained in said statistically identifying step (g).
- 5 3. A method according to Claim 1, wherein said statistically identifying step (g) uses linear regression analysis, multiple linear regression analysis, stepwise regression analysis, or partial least squares regression analysis.
4. A method according to Claim 1 or Claim 2, wherein said mathematical correlation in said statistically identifying step (g) comprises a linear function related to a near infrared absorbance peak of water in the  
 10 absorbance spectra of said multiple samples subjected to said pre-processing technique.
5. A method according to Claim 1 or Claim 2, wherein the biological matter is whole blood and the property of the first compartment to be analyzed is hematocrit or hemoglobin concentration in the whole blood.
6. A method according to Claim 1 or Claim 2, wherein the biological matter is whole blood and said absorbance peak of water occurs in the near infrared spectra from about 1150 to about 1190 nanometers,  
 15 and said another near infrared wavelength absorbance measuring point is the isosbestic point of oxyhemoglobin and deoxyhemoglobin.
7. A method according to Claim 2, wherein said detecting step (c) and said detecting step (j) use spectral analysis instrumentation which records said absorbance spectra of said multiple samples and said unknown sample in the dynamic condition of the biological matter flowing through the spectral analysis instrumenta-  
 20 tion.
8. A method according to Claim 2, wherein the property to be analyzed is hematocrit and said mathematical correlation solves the equation:  

$$Y = b + m * (\text{Absorbance at an Isosbestic Point of Deoxyhemoglobin and Oxyhemoglobin} / \text{Absorbance at said Absorbance Peak of Water})$$
  
 25 where Y is the value of hematocrit, b ranges from about -70 to about -128, and m ranges from about 78 to about 128.
9. A method according to Claim 2, wherein the property to be analyzed is hemoglobin concentration and said mathematical correlation solves the equation:  

$$Y = b + m * (\text{Absorbance at an Isosbestic Point of Deoxyhemoglobin and Oxyhemoglobin} / \text{Absorbance at said Absorbance Peak of Water})$$
  
 30 where Y is the hemoglobin concentration, b ranges from about -23 to about -45, and m ranges from about 26 to about 44.
10. A method according to Claim 1, further comprising the steps of:  
 (1) observing additional samples of biological matter in a dynamic condition;  
 35 (2) independently quantifying the property to be analyzed for each of said additional samples;  
 (3) performing steps (b), (c), and (d) with respect to said additional samples;  
 (4) predicting the property to be analyzed in said additional samples by utilizing said mathematical correlation obtained in said statistically identifying step (g); and  
 (5) validating said mathematical correlation by comparing the property predicted in step (4) to the  
 40 property independently quantified in step (2).
11. A method for the analysis of a biological fluid having a water content, in a dynamic condition, comprising:  
 observing multiple samples of a moving biological fluid of at least one organism, where the biological fluid may be approximated to comprise two compartments where one compartment has a proportionally different  
 45 amount of water than the other compartment which has a property of interest;  
 determining the two best absorbance detection points of the near infrared spectrum of each of said multiple samples;  
 independently measuring the quantity of the property to be analyzed in each of said multiple samples;  
 applying a ratio of said two best absorbance measuring points;  
 50 identifying a mathematical correlation of the property to be analyzed and the water content in the biological fluid; and  
 analyzing an unknown sample of the biological fluid to determine the property to be analyzed in said unknown sample by applying said mathematical correlation to a near infrared spectrum of said unknown sample.
- 55 12. A method for analyzing a property of whole animal blood having a water content, the whole animal blood comprising a first compartment related to the property to be analyzed and a second compartment having a proportionally larger or smaller amount of water than the first compartment, the method comprising:

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- (a) irradiating with near infrared light multiple samples of the whole animal blood;  
 (b) detecting the near infrared spectrum of each of said multiple samples;  
 (c) applying a pre-processing technique to the spectrum of each of said multiple samples;  
 (d) independently quantifying the property to be analyzed for each of said multiple samples;  
 5 (e) independently quantifying a value proportional to the percentage oxygen saturation in the whole animal blood for each of said multiple samples;  
 (f) establishing a training set from said near infrared spectra of said multiple samples; and  
 (g) statistically identifying the nature of a mathematical correlation between the property to be analyzed in the first compartment and the water content in the whole animal blood.
- 10 13. A method according to Claim 12, further comprising the steps of:  
 (h) irradiating an unknown sample of whole animal blood with near infrared light;  
 (i) detecting the near infrared spectrum of said unknown sample;  
 (j) applying said pre-processing technique to said spectrum of said unknown sample;  
 (k) determining a value proportional to the percent oxygen saturation of the unknown sample; and  
 15 (l) predicting the property to be analyzed in said unknown sample by utilizing said mathematical correlation obtained in said statistically identifying step (g).
14. A method according to Claim 12, wherein said statistically identifying step (g) uses multiple linear regression analysis, multiple stepwise regression analysis, partial least squares regression analysis and wherein said statistically identifying step (g) uses the independently quantified percent oxygen saturation in  
 20 said multiple samples as a regression variable in said analysis to determine said mathematical correlation.
15. A method according to Claim 12 or 13, wherein said mathematical correlation in said statistically identifying step (g) comprises a linear function related to a near infrared absorbance peak of water in the absorbance spectra of said multiple samples subjected to said pre-processing technique and the percent oxygen saturation in said multiple samples.
- 25 16. A method according to Claim 12 or 13, wherein said pre-processing technique comprises transforming said spectra of said multiple samples of said training set by computing a multiple derivative of said multiple samples.
17. A method according to Claim 12 or 13, wherein said pre-processing technique comprises applying a ratio of a near infrared wavelength absorbance peak of the water content in said training set to another near  
 30 infrared wavelength absorbance measuring point in said source spectra set.
18. A method according to Claim 12 or 13, wherein the property of the first compartment to be analyzed is hematocrit or hemoglobin concentration in the whole blood.
19. A method according to Claim 12 or 13, wherein said water content has an absorbance peak in the near  
 35 infrared spectra from about 1150 to about 1190 nanometers and the biological fluid has an isosbestic point of oxyhemoglobin and deoxyhemoglobin and wherein said pre-processing technique comprises applying a ratio of said water content absorbance peak to said isosbestic point.
20. A method according to Claim 13, wherein said detecting step (b) and said detecting step (i) use spectral analysis instrumentation which records said absorbance spectra of said multiple samples and said unknown  
 40 sample in the dynamic condition of the whole animal blood flowing through the spectral analysis instrumentation.
21. A method according to Claim 13, wherein the property to be analyzed is hematocrit and said mathematical correlation solves the equation:  

$$C = B_0 + B_1 (A_1) + B_2 (A_2)$$
 where C is the Hematocrit;  $B_0$  ranges from about -31 to about 32; where  $A_1$  is a value proportional to the  
 45 percent oxygen saturation and  $B_1$  is a regression coefficient for the percent oxygen saturation and ranges from about -0.4 to about 36; where  $A_2$  is a second derivative transformation of an absorbance peak of water and ranges from about 1160 to about 1175 nm and  $B_2$  is a regression coefficient of a second derivative transformation of said absorbance peak of water and ranges from about 439 to about 496.
22. A method according to Claim 13, wherein the property to be analyzed is concentration of hemoglobin  
 50 and said mathematical correlation solves the equation:  

$$C = B_0 + B_1 (A_1) + B_2 (A_2)$$
 where C is the concentration of hemoglobin;  $B_0$  ranges from about -11 to about 11; where  $A_1$  is a value proportional to the percent oxygen saturation and  $B_1$  is the regression coefficient for the percent oxygen saturation and ranges from about -0.08 to about 13; where  $A_2$  is a second derivative transformation of an  
 55 absorbance peak of water and ranges from about 1160 to about 1175 nm and  $B_2$  is a regression coefficient of a second derivative transformation of an absorbance peak of water and ranges from about 147 to about 169.
23. A method according to Claim 13, wherein the property to be analyzed is hematocrit and said

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mathematical correlation solves the equation:

$$C = B_0 + B_1 (A_1) + B_2 (A_2)$$

where C is the Hematocrit;  $B_0$  ranges from about -106 to about -134; where  $A_1$  is a value proportional to the percent oxygen saturation and  $B_1$  is a regression coefficient for the percent oxygen saturation and ranges from about -15 to about 0.1; where  $A_2$  is a ratio of the Absorbance at an Isosbestic Point of Deoxyhemoglobin and Oxyhemoglobin to an Absorbance at an Absorbance Peak of Water and  $B_2$  is a regression coefficient of an absorbance peak of water and ranges from about 116 to about 121.

24. A method according to Claim 13, wherein the property to be analyzed is hemoglobin concentration and said mathematical correlation solves the equation:

$$C = B_0 + B_1 (A_1) + B_2 (A_2)$$

where C is the concentration of hemoglobin;  $B_0$  ranges from about -46 to about -36; where  $A_1$  is a value proportional to the percent oxygen saturation and  $B_1$  is a regression coefficient for the percent oxygen saturation and ranges from about -5 to about 0.02; where  $A_2$  is a ratio of an Absorbance at an Isosbestic Point of Deoxyhemoglobin and Oxyhemoglobin to an Absorbance at an Absorbance Peak of Water and  $B_2$  is a regression coefficient of an absorbance peak of water and ranges from about 40 to about 42.

25. A method according to Claim 12 or 13, wherein said multiple samples are of at least one known organism of a given biological species.

26. A method according to Claim 13, wherein, to measure the percent oxygen saturation of the unknown sample, said determining step (k) comprises using a pulse oximeter, a co-oximeter, or the ratio of absorbances of two wavelengths where the ratio of extinction coefficients for oxyhemoglobin and deoxyhemoglobin at one wavelength is different than that ratio at the second wavelength.

27. A method according to Claim 12, further comprising the steps of:

- (1) observing additional samples of biological matter in a dynamic condition;
- (2) independently quantifying the property to be analyzed for each of said additional samples;
- (3) independently quantifying a value proportional to the percentage oxygen saturation in the whole animal blood for each of said additional samples;
- (4) performing steps (a), (b), and (c) with respect to said additional samples;
- (5) predicting the property to be analyzed in said additional samples by utilizing said mathematical correlation obtained in said statistically identifying step (g); and
- (6) validating by a statistical method said mathematical correlation by comparing the property predicted in step (5) to the property independently quantified in step (2).

28. A method for the analysis of a whole blood having a water content comprising:

observing multiple samples of whole blood of at least one organism, where the whole blood may be approximated to comprise two compartments where one compartment has a proportionally different amount of water than the other compartment which has a property of interest;

determining the best absorbance detection point comprising the absorbance peak of the water content in the near infrared spectrum of each of said multiple samples;

independently measuring the quantity of the property to be analyzed in each of said multiple samples and a value proportional to percent oxygen saturation of each of said multiple samples;

identifying a mathematical correlation of the property to be analyzed and the water content in the whole blood.

29. A method according to Claim 28, further comprising:

analyzing an unknown sample of the whole blood to determine the property to be analyzed in said unknown sample by applying said mathematical correlation to a near infrared spectrum of said unknown sample.

30. A method for monitoring a property of interest in whole blood of a live patient, nearly simultaneously with flow of the whole blood in the patient, comprising:

(a) establishing a blood flow loop having a diversion section departing from the patient terminating at a flow cell, a return section returning to the patient beginning at a flow cell, and a bypass section between the diversion section and the return section;

(b) flowing the whole blood through the blood loop;

(c) using near infrared detecting means to monitor the property of interest in the whole blood flowing through the blood loop; and

(d) identifying the value of the property of interest using a method of correlation of a linear functional relationship;

wherein said linear functional relationship comprises

- (1) observing multiple samples of whole blood of at least one organism, where the whole blood may be approximated to comprise two compartments where one compartment has a proportionally different amount of water than the other compartment which has the property of interest;

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(2) determining the best absorbance detection point comprising the absorbance peak of the water content in the near infrared spectrum of each of said multiple samples;

(3) independently measuring the quantity of the property to be analyzed in each of said multiple samples;

5 (4) identifying a mathematical correlation of the property to be analyzed and the water content in the whole blood.

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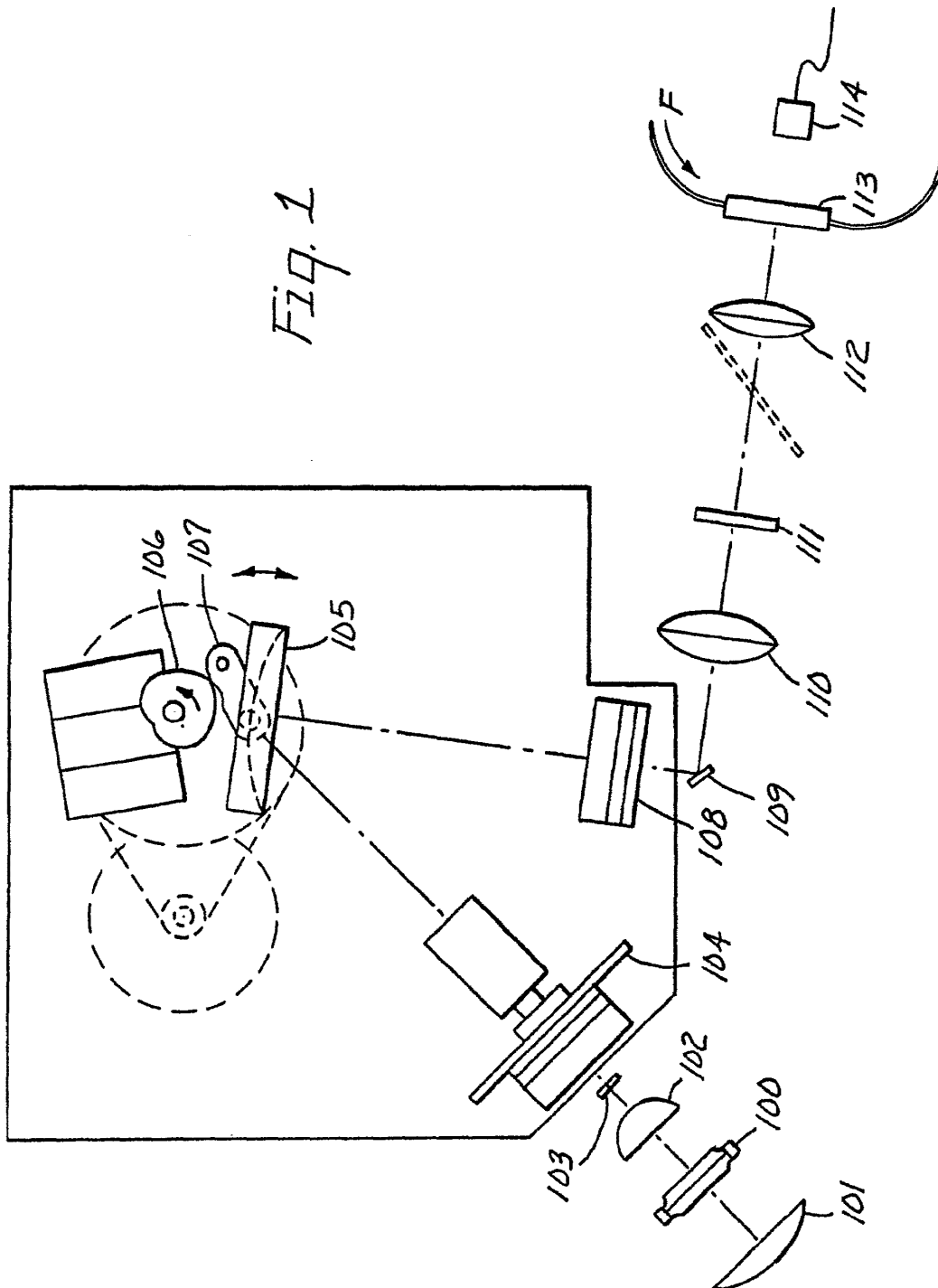
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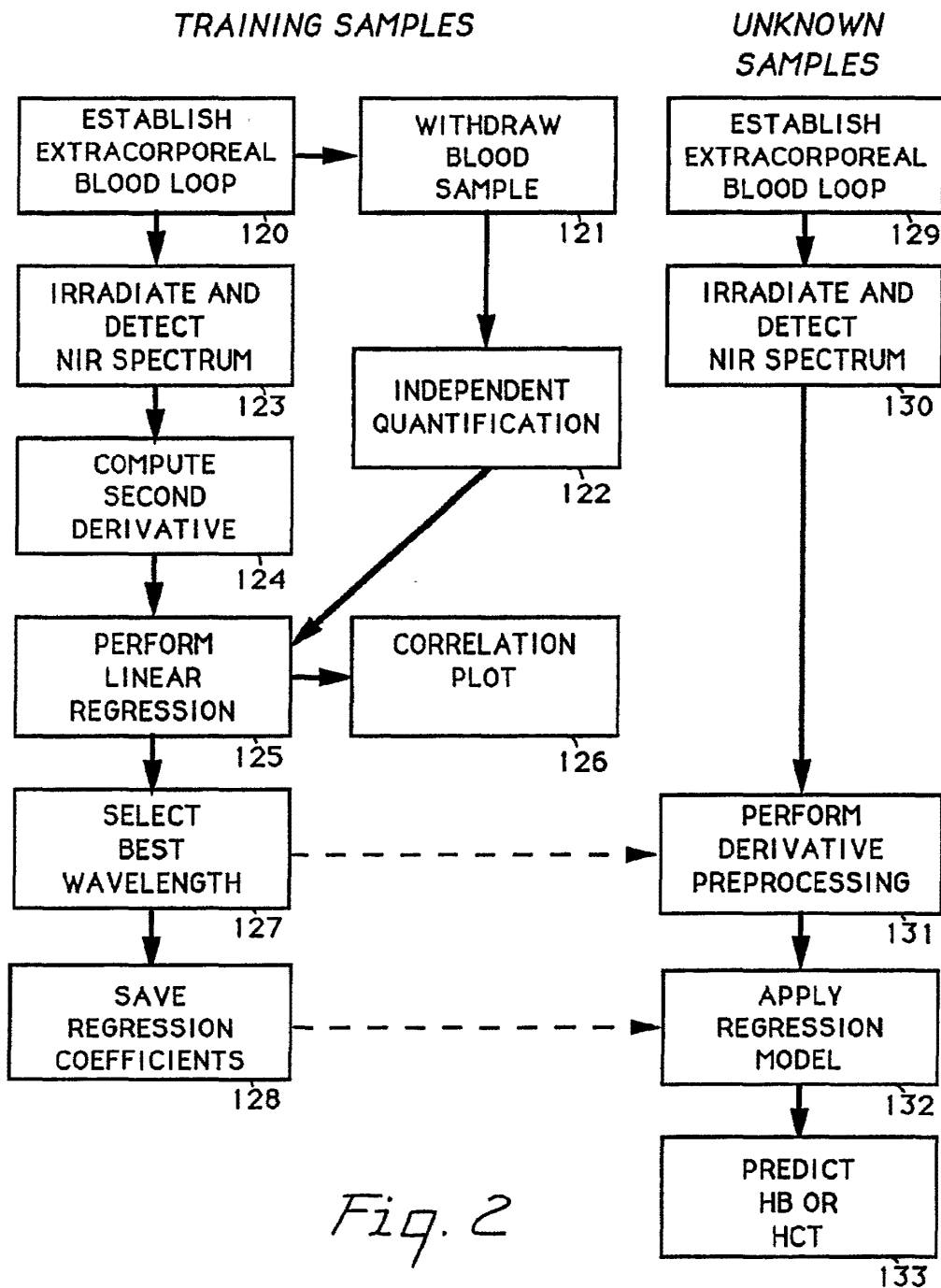
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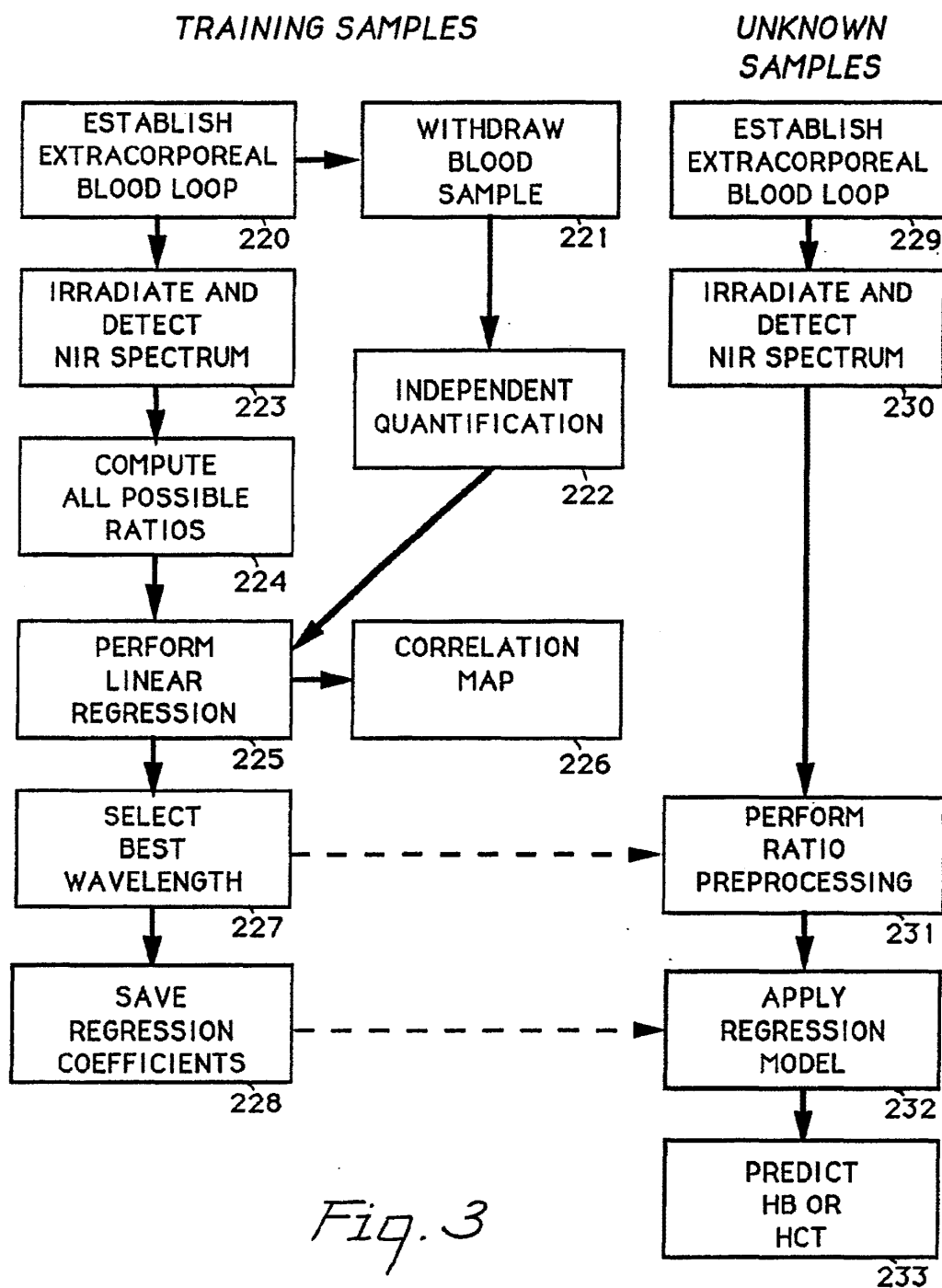
Fig. 1



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*Fig. 2*

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*Fig. 3*



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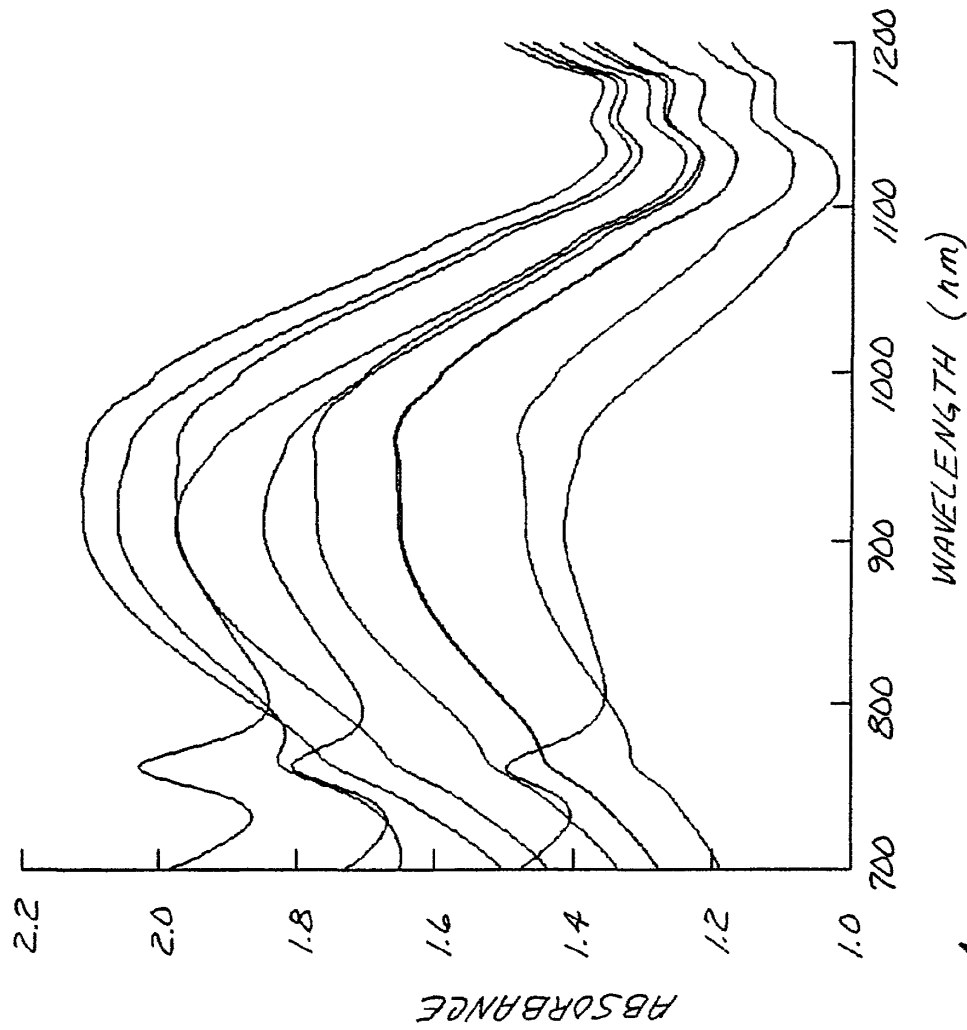


Fig. 4

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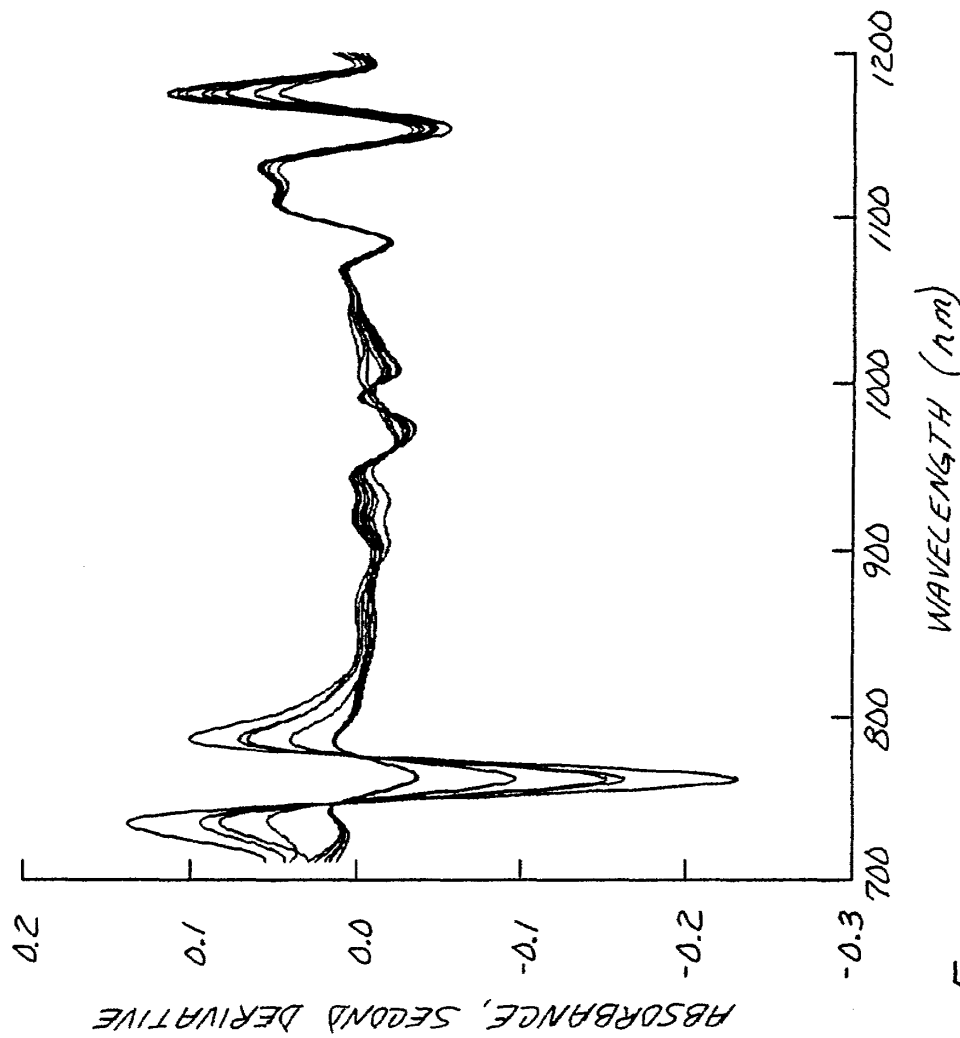


Fig. 5

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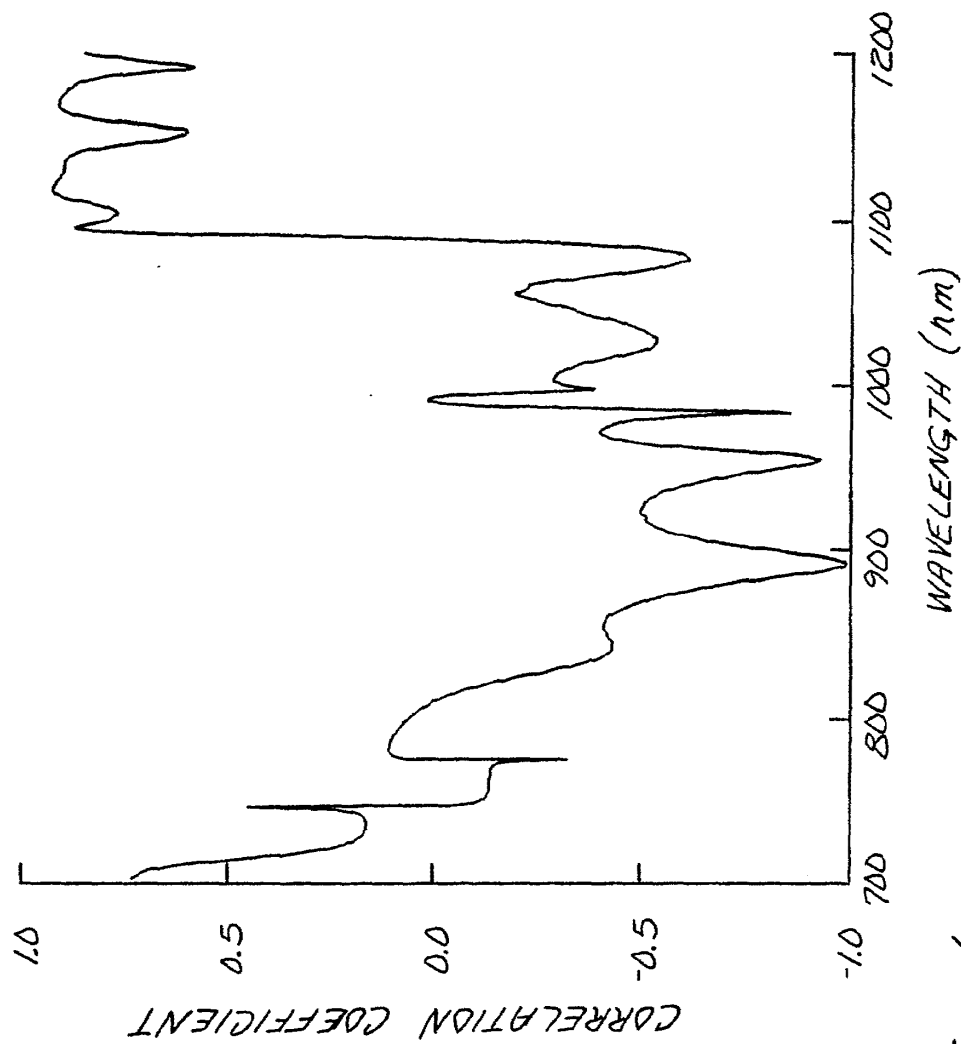


Fig. 6

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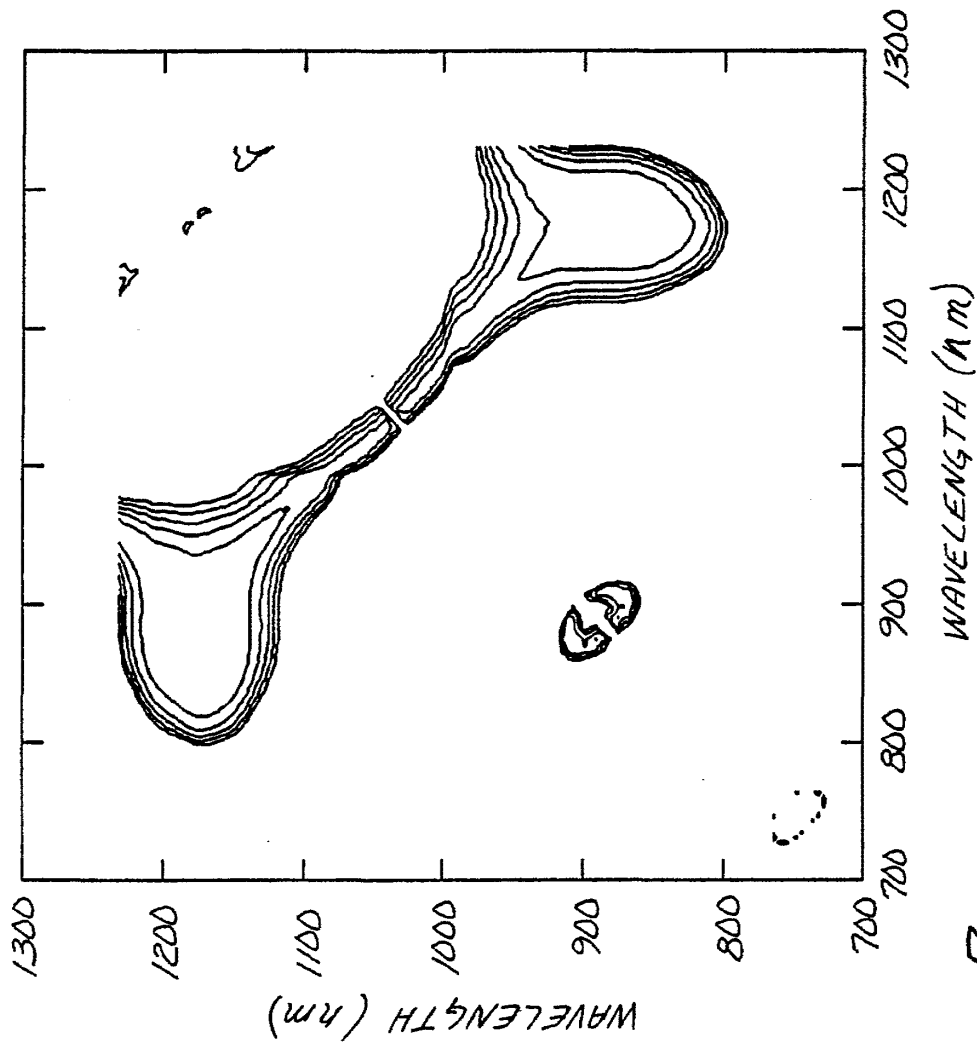


Fig. 7

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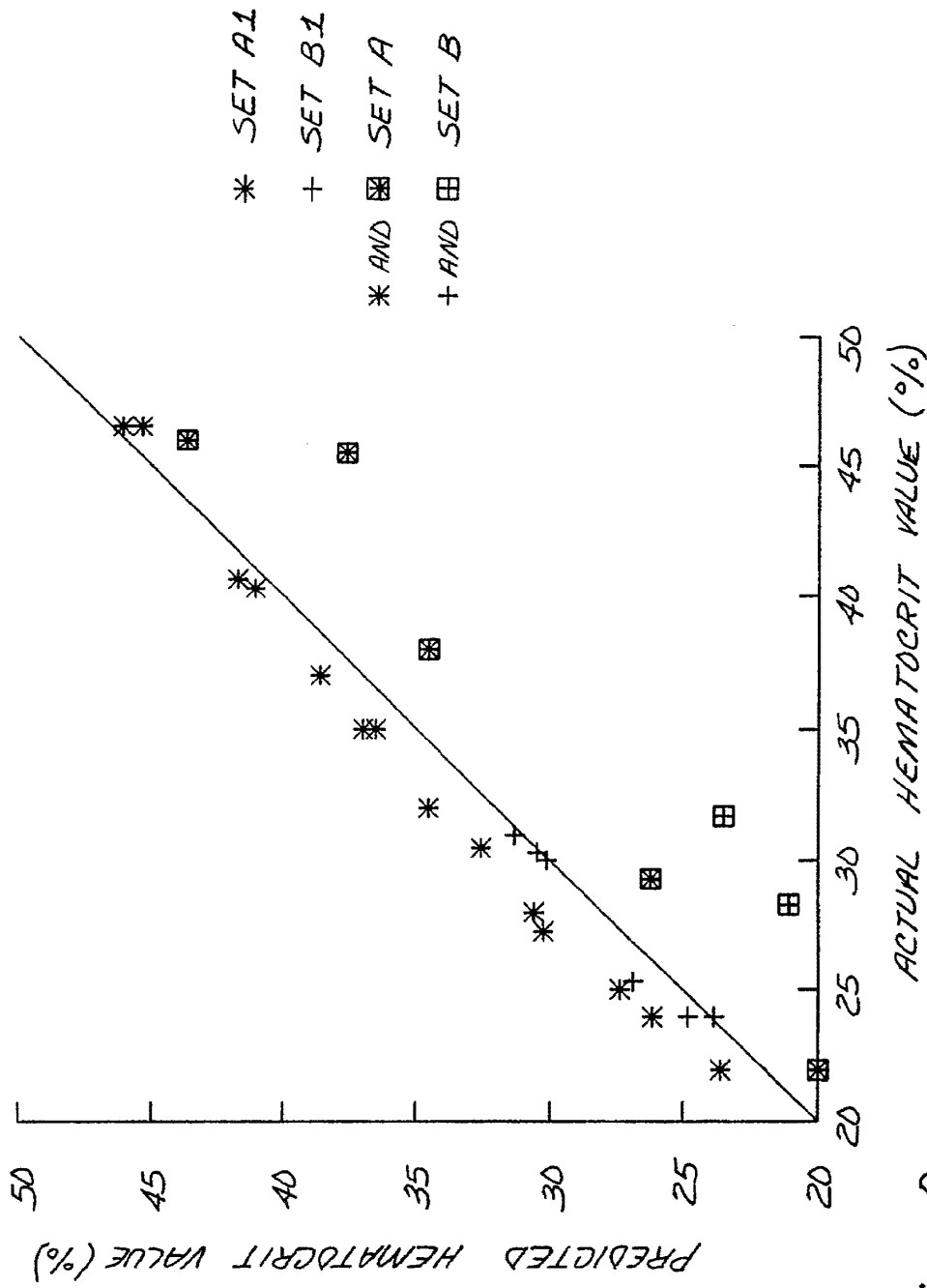


Fig. 8

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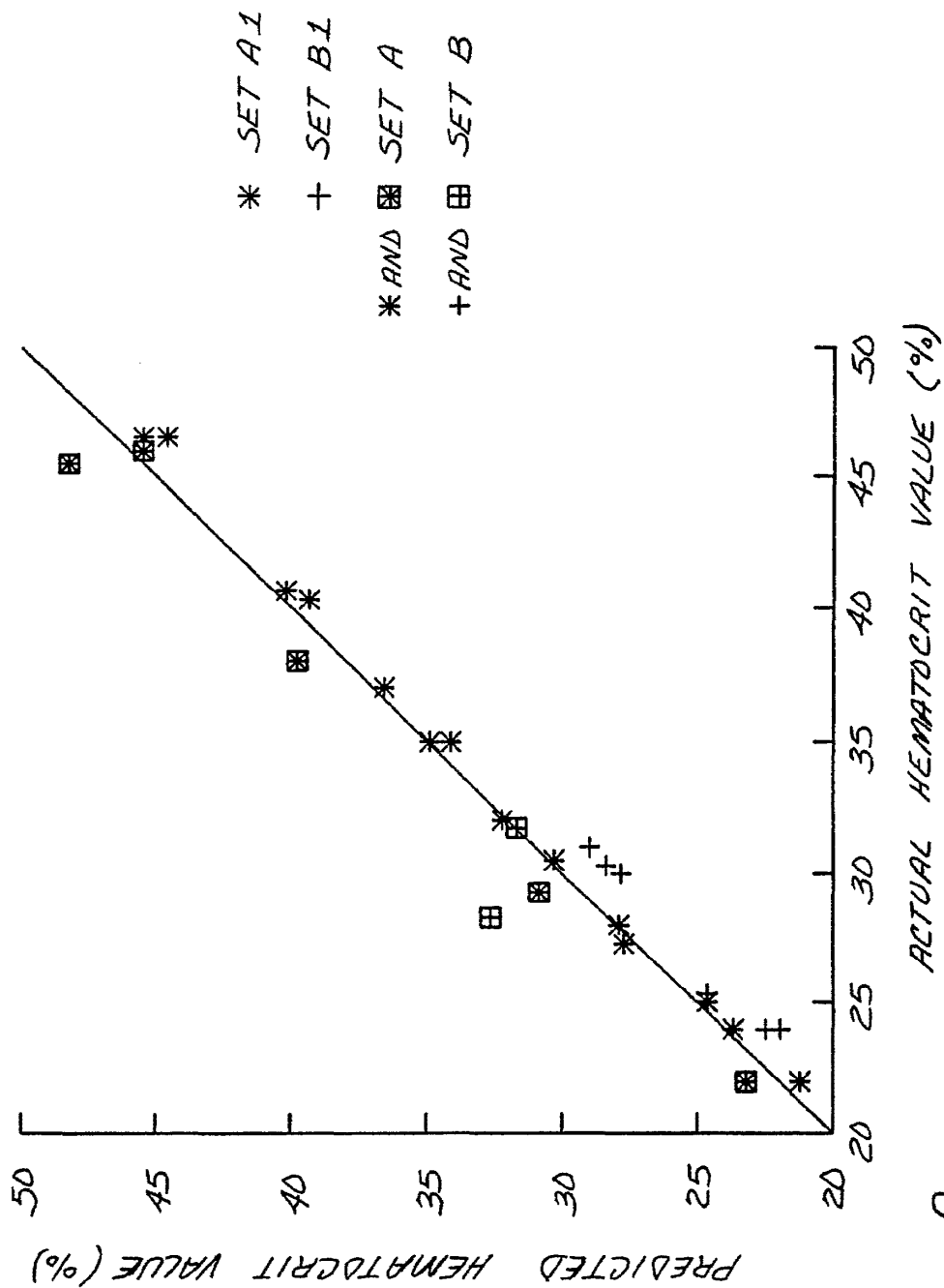
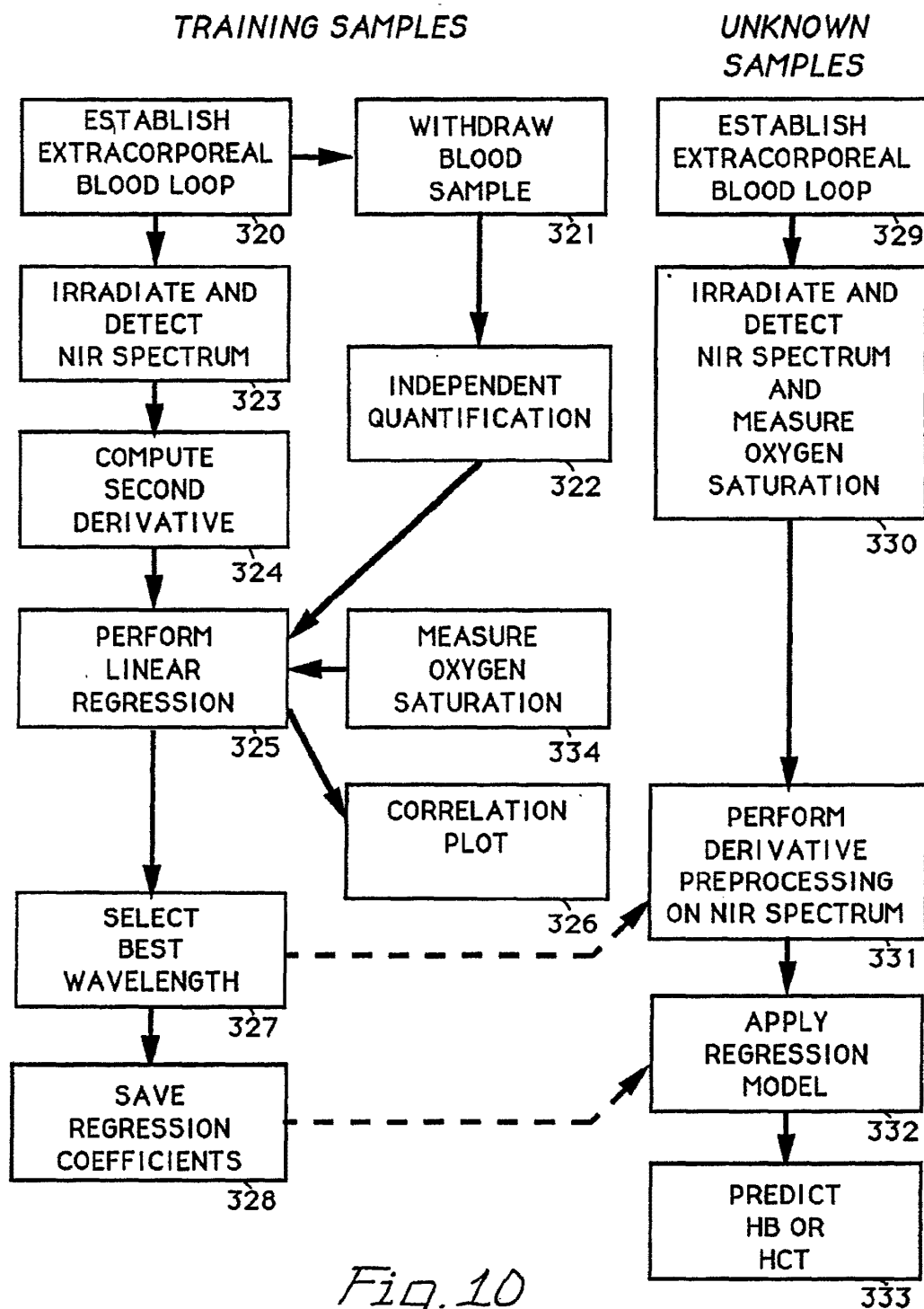
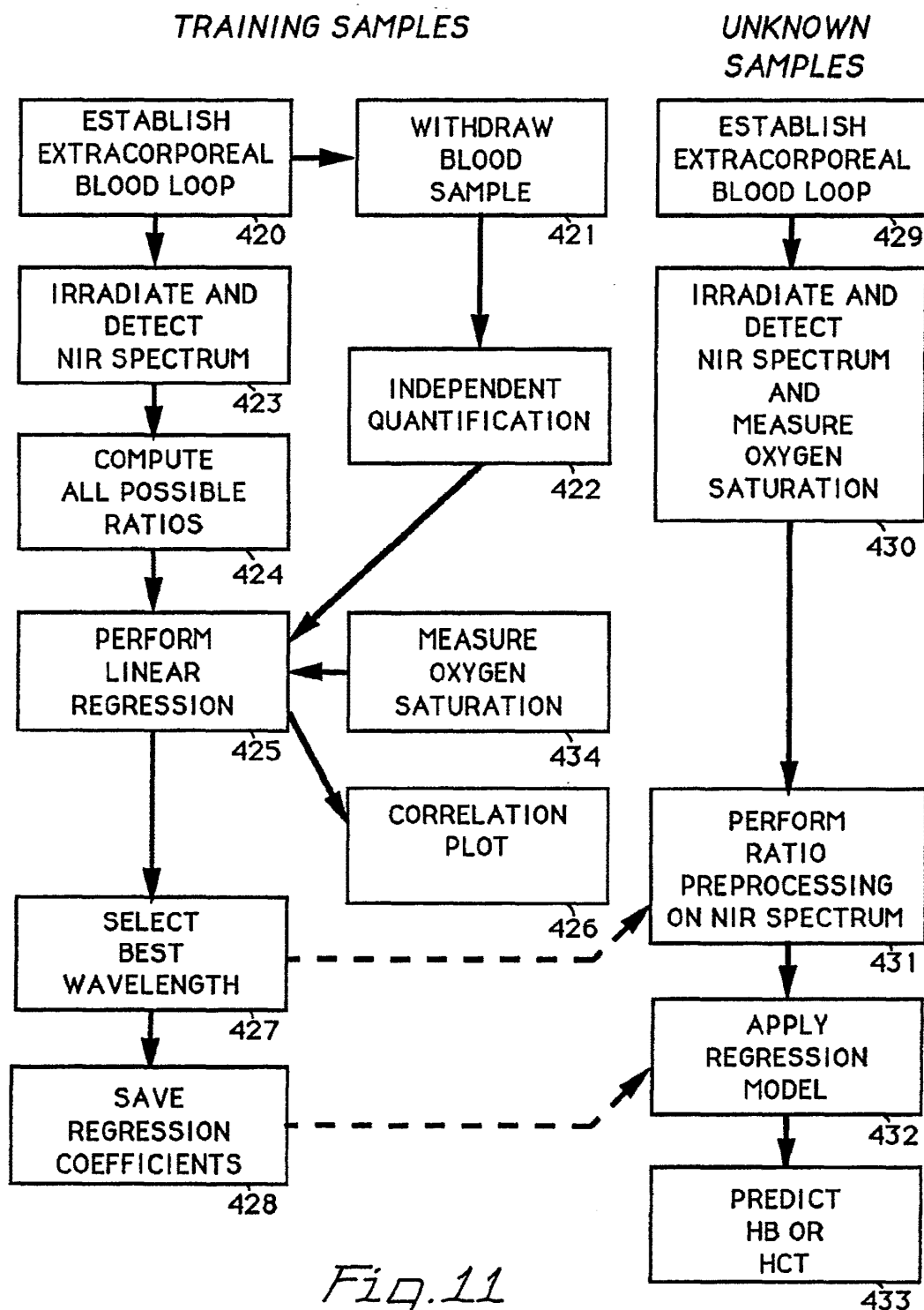


Fig. 9

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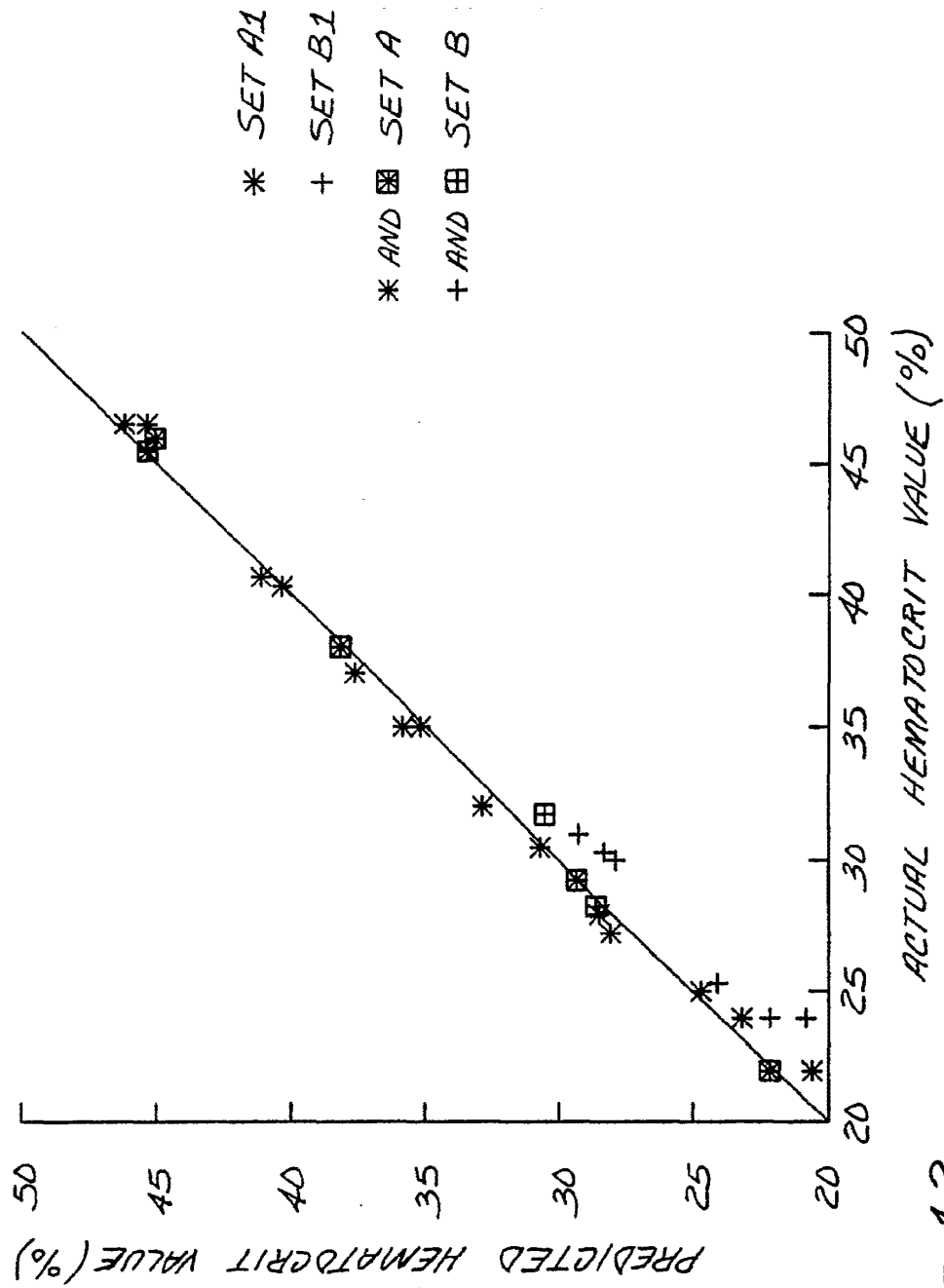


Fig. 12

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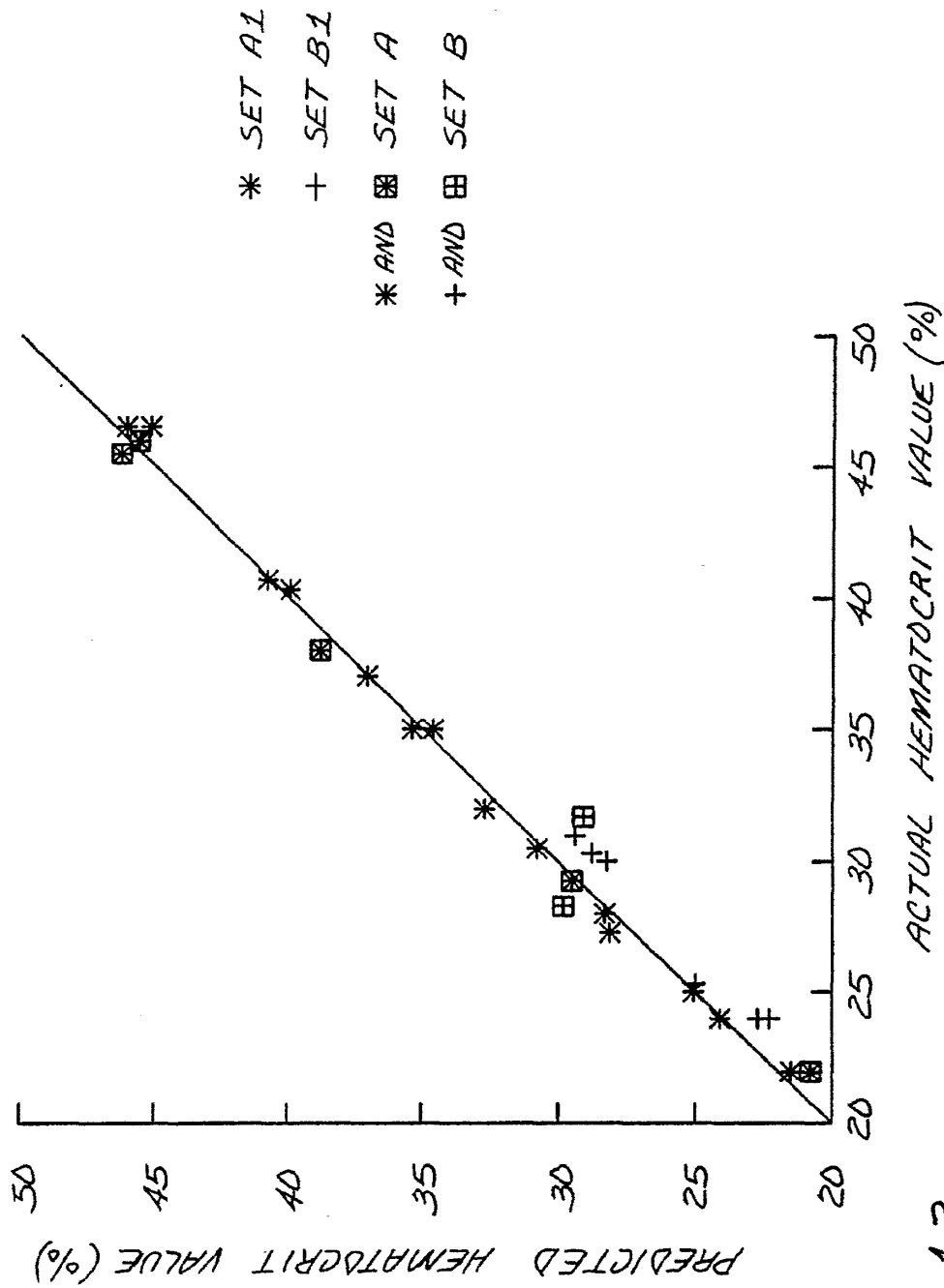


Fig. 13

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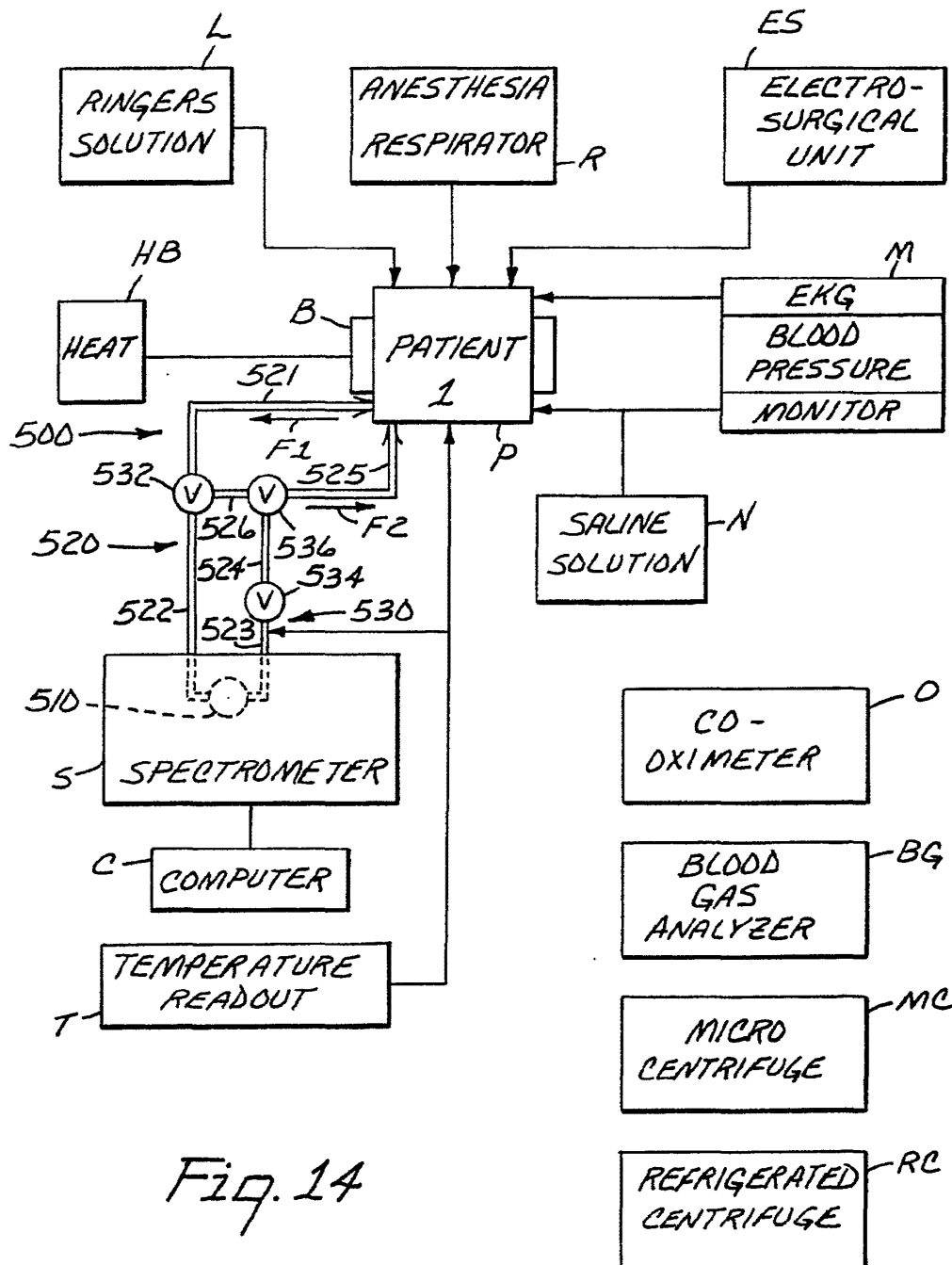


Fig. 14

Docket No.: MLHUM.002A

Customer No. 20995

**INFORMATION DISCLOSURE STATEMENT**

Applicant : Jeroen Poeze, et al.  
App. No : 12/534,827  
Filed : August 3, 2009  
For : MULTI-STREAM DATA  
COLLECTION SYSTEM FOR  
NONINVASIVE MEASUREMENT OF  
BLOOD CONSTITUENTS  
Examiner : Unknown  
Art Unit : 3768  
Conf No. : 1308

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Jarom D. Kesler, Reg. No. 57,046

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P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed for filing in the above-identified application is a PTO/SB/08 Equivalent listing 17 references, of which 9 are enclosed/submitted.

This Information Disclosure Statement is being filed before the receipt of a first Office Action on the merits, and presumably no fee is required. If a first Office Action on the merits was mailed before the mailing date of this Statement, the Commissioner is authorized to charge the fee set forth in 37 C.F.R. § 1.17(p) to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON &amp; BEAR, LLP

Dated: August 11, 2010

By:

Jarom D. Kesler  
Registration No. 57,046  
Attorney of Record  
Customer No. 20995  
(949) 760-0404

9489378

Docket No.: MLHUM.002A

Customer No. 20995

**INFORMATION DISCLOSURE STATEMENT**

Applicant : Jeroen Poeze, et al.  
App. No : 12/534,827  
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Examiner : Unknown  
Art Unit : 3768  
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Jarom D. Kesler, Reg. No. 57,046

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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed for filing in the above-identified application is a PTO/SB/08 Equivalent listing 242 references, of which 2 are enclosed/submitted.

This Information Disclosure Statement is being filed before the receipt of a first Office Action on the merits, and presumably no fee is required. If a first Office Action on the merits was mailed before the mailing date of this Statement, the Commissioner is authorized to charge the fee set forth in 37 C.F.R. § 1.17(p) to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: April 6, 2010

By:

Jarom D. Kesler  
Registration No. 57,046  
Attorney of Record  
Customer No. 20995  
(949) 760-0404

8836799

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827	
	Filing Date	08-03-2009	
	First Named Inventor	Poeze, Jeroen et al	
	Art Unit	3768	
(Multiple sheets used when necessary)		Examiner	Unknown
SHEET 1 OF 9		Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	6,345,194	02-05-2002	Robert Nelson, et al.	
	2	6,360,115	03-19-2002	Roger Greenwald, et al.	
	3	2004-054291	03-18-2004	Christian Schulz, et al.	
	4	2006-211924	09-21-2006	David Dalke, et al.	
	5	2009-0259114	10-15-2009	Johnson et al.	
	6	D609,193	02/2010	Al-Ali et al.	
	7	7,647,083	01/2010	Al-Ali et al.	
	8	D606,659	12/2009	Kiani et al.	
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	12	7,530,955	05/2009	Diab et al.	
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	20	7,499,835	03/2009	Weber et al.	
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	28	7,471,969	12/2008	Diab et al.	
	29	7,469,157	12/2008	Diab et al.	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

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CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
SHEET 2 OF 9		Attorney Docket No. MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	30	7,467,002	12/2008	Weber et al.	
	31	7,454,240	11/2008	Diab et al.	
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	33	7,438,683	10/2008	Al-Ali et al.	
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Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

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CX-1621

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
	Examiner	Unknown
SHEET 3 OF 9	Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
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	59	7,254,431	08/2007	Al-Ali	
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	87	6,993,371	01/2006	Kiani et al.	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.



CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
(Multiple sheets used when necessary)	Examiner	Unknown
SHEET 4 OF 9	Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	88	6,985,764	01/2006	Mason et al.	
	89	6,979,812	12/2005	Al-Ali	
	90	6,970,792	11/2005	Diab	
	91	6,961,598	11/2005	Diab	
	92	6,950,687	09/2005	Al-Ali	
	93	6,943,348	09/2005	Coffin IV	
	94	6,939,305	09/2005	Flaherty et al.	
	95	6,934,570	08/2005	Kiani et al.	
	96	6,931,268	08/2005	Kiani-Azarbayjany et al.	
	97	6,920,345	07/2005	Al-Ali et al.	
	98	6,898,452	05/2005	Al-Ali et al.	
	99	6,861,639	03/2005	Al-Ali	
	100	6,852,083	02/2005	Caro et al.	
	101	6,850,788	02/2005	Al-Ali	
	102	6,850,787	02/2005	Weber et al.	
	103	6,830,711	12/2004	Mills et al.	
	104	6,826,419	11/2004	Diab et al.	
	105	6,822,564	11/2004	Al-Ali	
	106	6,816,741	11/2004	Diab	
	107	6,813,511	11/2004	Diab et al.	
	108	6,792,300	09/2004	Diab et al.	
	109	6,771,994	08/2004	Kiani et al.	
	110	6,770,028	08/2004	Ali et al.	
	111	6,760,607	07/2004	Al-Ali	
	112	6,745,060	06/2004	Diab et al.	
	113	6,735,459	05/2004	Parker	
	114	6,728,560	04/2004	Kollias, et al.	
	115	6,725,075	04/2004	Al-Ali	
	116	6,721,585	04/2004	Parker	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Pocz, Jeroen et al
	Art Unit	3768
SHEET 5 OF 9		Attorney Docket No. MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	117	6,721,582	04/2004	Trepagnier, et al.	
	118	RE38,492	04/2004	Diab et al.	
	119	6,714,804	03/2004	Al-Ali et al.	
	120	RE38,476	03/2004	Diab et al.	
	121	6,699,194	03/2004	Diab et al.	
	122	6,697,658	02/2004	Al-Ali	
	123	6,697,657	02/2004	Shehada, et al.	
	124	6,697,656	02/2004	Al-Ali	
	125	6,684,091	01/2004	Parker	
	126	6,684,090	01/2004	Ali et al.	
	127	6,678,543	01/2004	Diab et al.	
	128	6,671,531	12/2003	Al-Ali et al.	
	129	6,661,161	12/2003	Lanzo et al.	
	130	6,658,276	12/2003	Diab et al.	
	131	6,654,624	11/2003	Diab et al.	
	132	6,650,917	11/2003	Diab et al.	
	133	6,643,530	11/2003	Diab et al.	
	134	6,640,116	10/2003	Diab	
	135	6,639,668	10/2003	Trepagnier, Pierre	
	136	6,632,181	10/2003	Flaherty et al.	
	137	6,606,511	08/2003	Ali et al.	
	138	6,597,933	07/2003	Kiani et al.	
	139	6,597,932	07/2003	Tian et al.	
	140	6,595,316	07/2003	Cybulski et al.	
	141	6,584,336	06/2003	Ali et al.	
	142	6,580,086	06/2003	Schulz et al.	
	143	6,542,764	04/2003	Al-Ali et al.	
	144	6,541,756	04/2003	Schulz et al.	
	145	6,526,300	02/2003	Kiani et al.	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

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CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827	
	Filing Date	08-03-2009	
	First Named Inventor	Poeze, Jeroen et al	
	Art Unit	3768	
(Multiple sheets used when necessary)		Examiner	Unknown
SHEET 6 OF 9		Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	146	6,525,386	02/2003	Mills et al.	
	147	6,519,487	02/2003	Parker	
	148	6,515,273	02/2003	Al-Ali	
	149	6,505,059	01/2003	Kollias, et al.	
	150	6,501,975	12/2002	Diab et al.	
	151	6,470,199	10/2002	Kopotic et al.	
	152	6,463,311	10/2002	Diab	
	153	6,430,525	08/2002	Weber et al.	
	154	6,397,091	05/2002	Diab et al.	
	155	6,388,240	05/2002	Schulz et al.	
	156	6,377,829	04/2002	Al-Ali	
	157	6,371,921	04/2002	Caro et al.	
	158	6,368,283	04/2002	Xu, et al.	
	159	6,360,114	03/2002	Diab et al.	
	160	6,349,228	02/2002	Kiani et al.	
	161	6,343,224	01/2002	Parker	
	162	6,334,065	12/2001	Al-Ali et al.	
	163	6,321,100	11/2001	Parker	
	164	6,285,896	09/2001	Tobler et al.	
	165	6,280,213	08/2001	Tobler et al.	
	166	6,278,522	08/2001	Lepper, Jr. et al.	
	167	6,263,222	07/2001	Diab et al.	
	168	6,256,523	07/2001	Diab et al.	
	169	6,241,683	06/2001	Macklem, et al.	
	170	6,236,872	05/2001	Diab et al.	
	171	6,232,609	05/2001	Snyder, et al.	
	172	6,229,856	05/2001	Diab et al.	
	173	6,206,830	03/2001	Diab et al.	
	174	6,184,521	02/2001	Coffin, IV et al.	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

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CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827	
	Filing Date	08-03-2009	
	First Named Inventor	Poeze, Jeroen et al	
	Art Unit	3768	
(Multiple sheets used when necessary)		Examiner	Unknown
SHEET 7 OF 9		Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	175	6,165,005	12/2000	Mills et al.	
	176	6,157,850	12/2000	Diab et al.	
	177	6,152,754	11/2000	Gerhardt et al.	
	178	6,151,516	11/2000	Kiani-Azarbayjany et al.	
	179	6,144,868	11/2000	Parker	
	180	6,124,597	09/2000	Shehada	
	181	6,110,522	08/2000	Lepper, Jr. et al.	
	182	6,088,607	07/2000	Diab et al.	
	183	6,081,735	06/2000	Diab et al.	
	184	6,067,462	05/2000	Diab et al.	
	185	6,045,509	04/2000	Caro et al.	
	186	6,036,642	03/2000	Diab et al.	
	187	6,027,452	02/2000	Flaherty et al.	
	188	6,011,986	01/2000	Diab et al.	
	189	6,002,952	12/1999	Diab et al.	
	190	5,997,343	12/1999	Mills et al.	
	191	5,995,855	11/1999	Kiani et al.	
	192	5,940,182	08/1999	Lepper, Jr. et al.	
	193	5,934,925	08/1999	Tobler et al.	
	194	5,919,134	07/1999	Diab	
	195	5,904,654	05/1999	Wohltmann et al.	
	196	5,890,929	04/1999	Mills et al.	
	197	5,860,919	01/1999	Kiani-Azarbayjany et al.	
	198	5,833,618	11/1998	Caro et al.	
	199	5,830,131	11/1998	Caro et al.	
	200	5,823,950	10/1998	Diab et al.	
	201	5,810,734	09/1998	Caro et al.	
	202	5,791,347	08/1998	Flaherty et al.	
	203	5,785,659	07/1998	Caro et al.	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

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CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
SHEET 8 OF 9		Attorney Docket No. MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	204	5,782,757	07/1998	Diab et al.	
	205	5,769,785	06/1998	Diab et al.	
	206	5,760,910	06/1998	Lepper, Jr. et al.	
	207	5,758,644	06/1998	Diab et al.	
	208	5,743,262	04/1998	Lepper, Jr. et al.	
	209	Des. 393,830	04/1998	Tobler et al.	
	210	5,685,299	11/1997	Diab et al.	
	211	5,645,440	07/1997	Tobler et al.	
	212	5,638,818	06/1997	Diab et al.	
	213	5,638,816	06/1997	Kiani-Azarbayjany et al.	
	214	5,632,272	05/1997	Diab et al.	
	215	5,602,924	02/1997	Durand et al.	
	216	5,590,649	01/1997	Caro et al.	
	217	5,562,002	10/1986	Lalin	
	218	5,561,275	10/1996	Savage, et al.	
	219	5,533,511	07/1996	Kaspari et al.	
	220	5,494,043	02/1996	O'Sullivan et al.	
	221	5,490,505	02/1996	Diab et al.	
	222	5,482,036	01/1996	Diab et al.	
	223	D363,120	10/1995	Savage et al.	
	224	5,456,252	10/1995	Vari, et al.	
	225	5,452,717	09/1995	Branigan et al.	
	226	D362,063	09/1995	Savage et al.	
	227	D361,840	08/1995	Savage et al.	
	228	D359,546	06/1995	Savage, et al.	
	229	5,431,170	07/1995	Mathews	
	230	D353,196	12/1994	Savage et al.	
	231	D353,195	12/1994	Savage et al.	
	232	5,278,627	01/1994	Aoyagi et al.	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

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CX-1621

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/534827
	Filing Date	08-03-2009
	First Named Inventor	Poeze, Jeroen et al
	Art Unit	3768
(Multiple sheets used when necessary)	Examiner	Unknown
SHEET 9 OF 9	Attorney Docket No.	MLHUM.002A

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	233	5,377,676	01/1995	Vari, et al.	
	234	5,341,805	08/1994	Stavridi, et al.	
	235	5,337,744	08/1994	Branigan	
	236	5,163,438	11/1992	Gordon et al.	
	237	5,069,213	12/1991	Polczynski	
	238	5,041,187	08/1991	Hink et al.	
	239	4,964,408	10/1990	Hink et al.	
	240	4,960,128	10/1990	Gordon et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>
	241	WO93/12712	07-08-1993	Vivascan Corp		

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	242	International Search Report and Written Opinion for PCT/US2009/049638, mailed January 7, 2010.	

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

**PCT**

To:

KNOBBE, MARTENS, OLSON  
Attn: Altman, Daniel E.  
AND BEAR, LLP  
2040 Main Street, Fourteenth Floor  
Irvine, CA 92614  
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
(day/month/year) 07/01/2010

Applicant's or agent's file reference

MLHUM.007VPC

**FOR FURTHER ACTION** See paragraphs 1 and 4 below

International application No.

PCT/US2009/049638

International filing date  
(day/month/year)

02/07/2009

Applicant

MASIMO LABORATORIES, INC.

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the International Search Report.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70

**For more detailed instructions,** see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

**4. Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, National Chapters.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Lars-Oliver Römich

**NOTES TO FORM PCT/ISA/220**

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

**INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19**

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annex B).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, International Phase, paragraph 296).

**What parts of the international application may be amended?**

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

**When?**

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

**Where not to file the amendments?**

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

**How?**

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet or sheets containing a complete set of claims in replacement of all the claims previously filed must be submitted.

Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively in Arabic numerals (Section 205(a)).

**The amendments must be made in the language in which the international application is to be published.**

**What documents must/may accompany the amendments?****Letter (Section 205(b)):**

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.**



**NOTES TO FORM PCT/ISA/220**

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

**INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19**

The applicant has, after having received the international search report and the written opinion of the International Searching Authority, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only (see *PCT Applicant's Guide*, Annex B).

The attention of the applicant is drawn to the fact that amendments to the claims under Article 19 are not allowed where the International Searching Authority has declared, under Article 17(2), that no international search report would be established (see *PCT Applicant's Guide*, International Phase, paragraph 296).

**What parts of the international application may be amended?**

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

**When?**

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

**Where not to file the amendments?**

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

**How?**

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet or sheets containing a complete set of claims in replacement of all the claims previously filed must be submitted.

Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively in Arabic numerals (Section 205(a)).

**The amendments must be made in the language in which the international application is to be published.**

**What documents must/may accompany the amendments?****Letter (Section 205(b)):**

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

**The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.**

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>MLHUM.007VPC</b>	<b>FOR FURTHER ACTION</b> see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. <b>PCT/US2009/049638</b>	International filing date (day/month/year) <b>02/07/2009</b>	(Earliest) Priority Date (day/month/year) <b>03/07/2008</b>
Applicant <b>MASIMO LABORATORIES, INC.</b>		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,

- ☒ the text is approved as submitted by the applicant  
☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- ☒ the text is approved as submitted by the applicant  
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. 2B

- ☒ as suggested by the applicant  
☐ as selected by this Authority, because the applicant failed to suggest a figure  
☐ as selected by this Authority, because this figure better characterizes the invention

b. ☐ none of the figures is to be published with the abstract

Form PCT/ISA/210 (first sheet) (April 2007)

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2009/049638

**A. CLASSIFICATION OF SUBJECT MATTER**  
INV. A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/054291 A1 (SCHULZ CHRISTIAN [US] ET AL) 18 March 2004 (2004-03-18) paragraphs [0003], [0007], [0036], [0037], [0042], [0065] - [0068]	1-21
X	US 6 345 194 B1 (NELSON ROBERT S [US] ET AL) 5 February 2002 (2002-02-05) abstract column 1, line 31 - column 2, line 9 column 3, lines 14-23 column 9, line 63 - column 10, line 44 column 11, lines 36-58 column 13, lines 15-40 ----- -/--	1

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

## \* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

21 September 2009

Date of mailing of the international search report

07/01/2010

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040.  
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Authorized officer

Ferrigno, Antonio

CX-1621

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2009/049638

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93/12712 A (VIVASCAN CORP [US]) 8 July 1993 (1993-07-08) abstract page 6, line 22 - page 7, line 25 page 10, line 11 - page 11, line 3 -----	1
A	US 6 360 115 B1 (GREENWALD ROGER J [US] ET AL) 19 March 2002 (2002-03-19) abstract column 2, line 49 - column 3, line 37 -----	1,10,13
A	US 2006/211924 A1 (DALKE DAVID [US] ET AL) 21 September 2006 (2006-09-21) cited in the application abstract paragraphs [0007], [0064] -----	1,15

3

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2009/049638**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-21

**Remark on Protest**

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

International Application No. PCT/US2009 /049638

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-21

physiological sensor with means to reduce thickness of body tissue  
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2. claims: 22-31

physiological sensor with a heat sink  
---

3. claims: 32-38

heat sink of a medical sensor  
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4. claims: 39-46

conductive shield for a light sensitive detector  
---

5. claims: 47-53

optical sensor comprising a noise shield  
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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2009/049638

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004054291	A1	18-03-2004	NONE
US 6345194	B1	05-02-2002	NONE
WO 9312712	A	08-07-1993	AU 2245092 A 28-07-1993 JP 2637344 B2 06-08-1997 JP 6290307 A 18-10-1994 US 5372135 A 13-12-1994
US 6360115	B1	19-03-2002	AU 8908798 A 08-03-1999 EP 1005288 A1 07-06-2000 WO 9908588 A1 25-02-1999 US 5978695 A 02-11-1999
US 2006211924	A1	21-09-2006	EP 1860989 A1 05-12-2007 EP 1860990 A1 05-12-2007 EP 1860991 A1 05-12-2007 EP 1860992 A1 05-12-2007 EP 1863380 A2 12-12-2007 EP 1860993 A1 05-12-2007 EP 1860994 A1 05-12-2007 EP 1860995 A1 05-12-2007 EP 1860996 A1 05-12-2007 EP 1895892 A1 12-03-2008 EP 1860997 A1 05-12-2007 JP 2008531211 T 14-08-2008 JP 2008531212 T 14-08-2008 JP 2008535540 T 04-09-2008 JP 2008531214 T 14-08-2008 JP 2008531215 T 14-08-2008 JP 2008532589 T 21-08-2008 JP 2008538186 T 16-10-2008 JP 2008531216 T 14-08-2008 JP 2008531217 T 14-08-2008 JP 2008531218 T 14-08-2008 JP 2008531225 T 14-08-2008 US 2008220633 A1 11-09-2008 US 2006220881 A1 05-10-2006 US 2006211922 A1 21-09-2006 US 2006241358 A1 26-10-2006 US 2006229509 A1 12-10-2006 US 2006211923 A1 21-09-2006 US 2006241363 A1 26-10-2006 US 2006238358 A1 26-10-2006 US 2006226992 A1 12-10-2006 US 2006211925 A1 21-09-2006 US 2006211932 A1 21-09-2006 WO 2006094107 A1 08-09-2006 WO 2006094108 A1 08-09-2006 WO 2006094109 A1 08-09-2006 WO 2006094155 A1 08-09-2006 WO 2006115580 A2 02-11-2006 WO 2006094168 A1 08-09-2006 WO 2006094169 A1 08-09-2006 WO 2006094170 A1 08-09-2006 WO 2006094171 A1 08-09-2006 WO 2006118654 A1 09-11-2006 WO 2006094279 A1 08-09-2006

Form PCT/SA/210 (patent family annex) (April 2005)

**PATENT COOPERATION TREATY**From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

**PCT****WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)**Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)Applicant's or agent's file reference  
see form PCT/ISA/220**FOR FURTHER ACTION**  
See paragraph 2 belowInternational application No.  
PCT/US2009/049638International filing date (day/month/year)  
02.07.2009Priority date (day/month/year)  
03.07.2008International Patent Classification (IPC) or both national classification and IPC  
INV. A61B5/00Applicant  
MASIMO LABORATORIES, INC.**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA:



European Patent Office  
P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040  
Fax: +31 70 340 - 3016

Date of completion of  
this opinionsee form  
PCT/ISA/210

Authorized Officer

Ferrigno, Antonio

Telephone No. +31 70 340-2174





**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/049638

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of:
  - ☒ the international application in the language in which it was filed
  - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ on paper
    - ☐ in electronic form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in electronic form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/049638**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 22-53

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for the whole application or for said claims Nos. 22-53

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13<sup>ter</sup>.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**International application No.  
PCT/US2009/049638**Box No. IV Lack of unity of invention**

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☐ paid additional fees
  - ☐ paid additional fees under protest and, where applicable, the protest fee
  - ☐ paid additional fees under protest but the applicable protest fee was not paid
  - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
  - ☒ not complied with for the following reasons:  
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
  - ☒ the parts relating to claims Nos. 1-21

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. Statement

Novelty (N)	Yes: Claims	<u>3-8</u>
	No: Claims	<u>1,2,9-21</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-21</u>
Industrial applicability (IA)	Yes: Claims	<u>1-21</u>
	No: Claims	

## 2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/049638

**Re Item III.**

Claims 22-53 not searched: see **Re Item IV** below.

**Re Item IV.**

The separate inventions/groups of inventions are:

1-21

physiological sensor with means to reduce thickness of body tissue

22-31

physiological sensor with a heat sink

32-38

heat sink of a medical sensor

39-46

conductive shield for a light sensitive detector

47-53

optical sensor comprising a noise shield

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

Document US2006/0211924 discloses (cf passages cited in the search report) the common features of claims 1 and 15. The remaining features are a bump as recited in claim 1, and a partially cylindrical lens as recited in claim 15. These features solve the problem of reducing thickness of body tissue and can be considered the first invention.

The subject-matter of claim 22 differs from the disclosure of document US2006/0211924 in that a heat sink is provided as recited in claim 22. This feature solves the problem of cooling the optical source and can be considered a second different invention.

The subject-matter of claim 32 is directed to an heat sink and doesn't have any feature in common with claims 1 and 15. It also doesn't have any feature in common with the subject-matter of claim 22, other than a "heat sink" (which is generally a known device). It solves the problem of providing an efficient heat sink and therefore can be

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

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considered a third different invention.

The subject-matter of claim 39 is directed to a conductive shield and doesn't have any feature in common with claims 1, 15, 22 and 32. It solves the problem of providing an efficient noise shielding device and therefore can be considered a fourth different invention.

Document US2006/0211924 discloses (cf passages cited in the search report) the common features of claims 1, 15, 22, and 47. Claim 47 provides the extra feature of a conductive shield. Claim 47 doesn't have any feature in common with claim 32. It also doesn't have any feature in common with claim 39, other than a "conductive shield" (which is generally a known device). The conductive shield, as recited in claim 47, solves the problem of protecting the sensor from noise interference and therefore can be considered a fifth different invention.

**Re Item V.**

1 Reference is made to the following documents:

- D1: US 2004/054291 A1 (SCHULZ CHRISTIAN [US] ET AL) 18 March 2004  
(2004-03-18)
- D2: US-B1-6 345 194 (NELSON ROBERT S [US] ET AL) 5 February 2002  
(2002-02-05)
- D3: WO 93/12712 A (VIVASCAN CORP [US]) 8 July 1993 (1993-07-08)

2 INDEPENDENT CLAIM 1

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.

Document D1 discloses (the references in parentheses applying to this document):

a noninvasive physiological sensor (1900, cf. paragraph 65 and figures 19A-D) for

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2009/049638

measuring one or more physiological parameters of a medical patient, the sensor comprising:

- a light source (not shown in these figure; cf. paragraph 35 and claim 1);
- a photodetector (not shown in these figure; cf. paragraph 35 and claim 1) operative to detect light from said light source after attenuation by body tissue of a medical patient and to generate a physiological signal responsive to the detected light, the physiological signal reflecting one or more physiological parameters of the medical patient (cf. paragraph 3); and
- a bump (1920,1921) interposed between the light source and the photodetector, the bump protruding from a tissue contacting surface, the bump configured to reduce a thickness of the body tissue between the light source and the photodetector such that an optical pathlength between the light source and the photodetector is reduced (see spring 1910).

Hence, the subject-matter of claim 1 is disclosed in document D1.

- 2.2 The subject-matter of claim 1 is also disclosed in documents D2 and D3 (see corresponding passages cited in the search report: although the device disclosed in D2 is used for image mammography, it is also suitable to be used with other processing devices, and therefore for measuring one or more physiological parameters of a medical patient).

### 3 INDEPENDENT CLAIM 15

- 3.1 The bumps (1920,1921) disclosed in document D1 are partially cylindrical lenses (see paragraph 68). Hence, the same reasoning applies, *mutatis mutandis*, to the subject-matter of independent claim 15, which therefore is also considered not new.

### 4 DEPENDENT CLAIMS 2-14, 16-21

- 4.1 For the same reasons also the subject-matter of dependent claim 2 is considered not new.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

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- 4.2 The additional features of dependent claims 9, 10, 18-21 attempt to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result (Article 6 PCT). However these features appear to be disclosed in document D1 (see passages cited in the search report). Hence, also the subject-matter of these claims is considered not new.
- 4.3 The additional features of dependent claims 11-14, 16, and 17 are also disclosed in document D1 (see passages cited in the search report). Hence, also the subject-matter of these claims is considered not new.
- 4.4 The additional features of dependent claims 3-8 are just some dimensional straightforward possibilities which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill (Articles 33(1) and 33(3) PCT).

**Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO-ISA)**

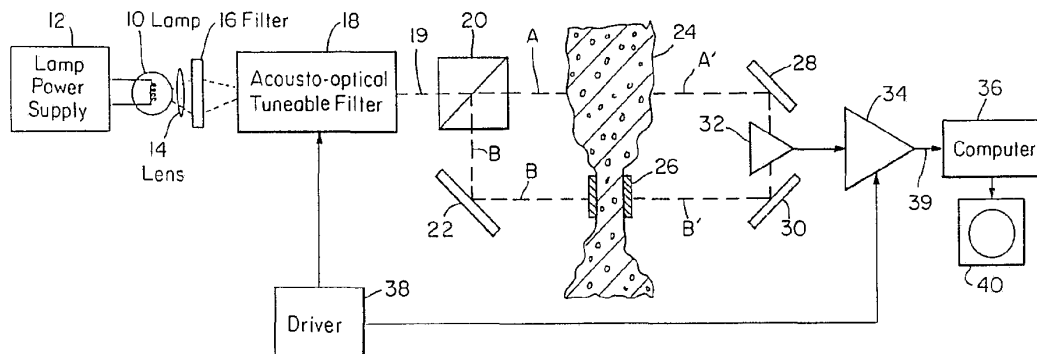
General information	For all international applications filed on or after 01/01/2004 the competent ISA will establish an ISR. It is accompanied by the WO-ISA. Unlike the former written opinion of the IPEA (Rule 66.2 PCT), the WO-ISA is not meant to be responded to, but to be taken into consideration for further procedural steps. This document explains about the possibilities.
Amending claims under Art. 19 PCT	Within 2 months after the date of mailing of the ISR and the WO-ISA the applicant may file amended claims under Art. 19 PCT directly with the International Bureau of WIPO. The PCT reform of 2004 did not change this procedure. For further information please see Rule 46 PCT as well as form PCT/ISA/220 and the corresponding Notes to form PCT/ISA/220.
Filing a demand for international preliminary examination	<p>In principle, the WO-ISA will be considered as the written opinion of the IPEA. This should, in many cases, make it unnecessary to file a demand for international preliminary examination. If the applicant nevertheless wishes to file a demand this must be done before expiry of 3 months after the date of mailing of the ISR/ WO-ISA or 22 months after priority date, whichever expires later (Rule 54bis PCT). Amendments under Art. 34 PCT can be filed with the IPEA as before, normally at the same time as filing the demand (Rule 66.1 (b) PCT).</p> <p>If a demand for international preliminary examination is filed and no comments/amendments have been received the WO-ISA will be transformed by the IPEA into an IPRP (International Preliminary Report on Patentability) which would merely reflect the content of the WO-ISA. The demand can still be withdrawn (Art. 37 PCT).</p>
Filing informal comments	After receipt of the ISR/WO-ISA the applicant may file informal comments on the WO-ISA directly with the International Bureau of WIPO. These will be communicated to the designated Offices together with the IPRP (International Preliminary Report on Patentability) at 30 months from the priority date. Please also refer to the next box.
End of the international phase	At the end of the international phase the International Bureau of WIPO will transform the WO-ISA or, if a demand was filed, the written opinion of the IPEA into the IPRP, which will then be transmitted together with possible informal comments to the designated Offices. The IPRP replaces the former IPER (international preliminary examination report).
Relevant PCT Rules and more information	Rule 43 PCT, Rule 43bis PCT, Rule 44 PCT, Rule 44bis PCT, PCT Newsletter 12/2003, OJ 11/2003, OJ 12/2003



**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification 5 :</b> <b>A61B 5/00, G01N 21/31</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 93/12712</b> <b>(43) International Publication Date:</b> 8 July 1993 (08.07.93)
<b>(21) International Application Number:</b> PCT/US92/01330 <b>(22) International Filing Date:</b> 19 February 1992 (19.02.92) <b>(30) Priority data:</b> 815,469 31 December 1991 (31.12.91) US <b>(71) Applicant:</b> VIVASCAN CORPORATION [US/US]; 22 High Street, Southborough, MA 01772 (US). <b>(72) Inventor:</b> MENDELSON, Yitzhak ; 31 Whisper Drive, Worcester, MA 01609 (US). <b>(74) Agents:</b> REYNOLDS, Leo, R. et al.; Hamilton, Brook, Smith & Reynolds, Two Militia Drive, Lexington, MA 02173 (US).		<b>(81) Designated States:</b> AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MW, NL, NO, PL, RO, RU, SD, SE, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>

**(54) Title:** BLOOD CONSTITUENT DETERMINATION BASED ON DIFFERENTIAL SPECTRAL ANALYSIS**(57) Abstract**

The present invention relates to the determination of an analyte or multiple analytes in blood using information derived from the differential optical absorption spectra of blood. Specifically, the information is derived from the differential spectra of tissue before and immediately after the volume of blood in the tissue has been changed.

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FR	France	MR	Mauritania
AU	Australia	GA	Gabon	MW	Malawi
BB	Barbados	GB	United Kingdom	NL	Netherlands
BE	Belgium	GN	Guinea	NO	Norway
BF	Burkina Faso	GR	Greece	NZ	New Zealand
BG	Bulgaria	HU	Hungary	PL	Poland
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BLOOD CONSTITUENT DETERMINATION BASED ON  
DIFFERENTIAL SPECTRAL ANALYSIS

Field of the Invention

This invention relates to instrumentation and methods  
5 for noninvasive quantitative measurement of biochemical  
blood constituents such as blood glucose, urea,  
cholesterol, etc.

Background of the Invention

The determination of blood glucose is critical to  
10 diabetic patients. These patients must measure their blood  
glucose level several times daily in order to determine how  
much insulin their body requires. For diabetics with  
internally implantable or external insulin pumps, the  
ability to have a reliable glucose sensor that can  
15 continuously measure their blood glucose is essential for  
the realization of an artificial pancreas device.

Considerable efforts have been placed on the  
development of reliable methods for measuring blood glucose  
noninvasively. Although several sensors have been  
20 successfully developed for in vitro and in vivo  
applications, these sensors can be used only for  
intermittent measurements or short term monitoring. None  
of these devices are suitable for long-term in vivo  
applications utilizing noninvasive means.

25 The concentration of a limited number of analytes in  
blood can be measured noninvasively by spectroscopic means.  
For instance, by measuring the amount of optical radiation  
either absorbed by, transmitted through or reflected from  
biological tissues, it is possible to derive a quantitative  
30 measurement relative to the concentration of oxygen in  
blood. In contrast to invasive measurement, noninvasive

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measurements are clearly more attractive because they are safe, fast, convenient, painless and can be used to provide short-term and long-term continuous information on changing levels of blood analytes in the body. Therefore,

- 5 noninvasive measurement of blood constituents is desirable, especially in children and older patients.

Several attempts have been made in the past to develop a reliable method for quantitative noninvasive measurement of glucose levels in biological tissues by irradiating the  
10 tissue with light at predetermined wavelengths and using the principle of absorption spectroscopy. Some methods are based on detecting the resonance absorption peaks in the infrared region of the electromagnetic spectrum, also known as the "fingerprints" region, which are caused by  
15 vibrational and rotational oscillations of the molecules and are characteristic for different molecules. Other techniques are based upon near-infrared spectroscopy to determine the sample's composition. Unlike the  
"fingerprint" region, which is valuable as a tool for  
20 obtaining structural information on the sample, structural measurements in the near infrared region of the spectra are obscured because of multiple and weak overtones yielding many overlapping peaks.

Regardless of which spectroscopic method is employed,  
25 there are four basic practical difficulties which limit the noninvasive detection of most biological substances including glucose: 1) The high intrinsic background absorption by water, 2) the relatively low concentration of most biological substances, 3) the number of weak and  
30 overlapping absorption peaks in the spectra, and 4) the highly scattering properties of biological tissues.

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Moreover, the large variations in the optical properties of skin among different individuals makes absolute measurements and calibrations very difficult and impractical.

5 Two methods are commonly utilized for obtaining spectral information from biological tissues for the purpose of measuring the concentration of various biochemical constituents noninvasively. One method is based on information derived from the absolute optical  
10 spectra of tissues containing blood. According to this concept, the tissue is illuminated with light at different preselected wavelengths and either the total or proportional amount of light which is transmitted through, reflected from, or transflected by the tissue is measured  
15 by a photodetector. This technique was utilized for example by Hewlett-Packard in their ear oximeter product (U.S. Patent 3,638,648 by Shaw) and by Rosenthal et al. (U.S. Patent 5,028,787). According to the other method, which is widely used in pulse oximetry, the tissue is  
20 illuminated by two different light sources. Typically, one wavelength around 660 nm and the other in the range between 815 nm and 960 nm are used. The change in optical absorption caused by the pulsation of arterial blood in the tissue is measured and analyzed to provide a quantitative  
25 measure of the amount of oxygen present in the arterial blood. According to this second technique, the ratio between the normalized pulsatile and nonpulsatile components of a single pair of red and infrared wavelengths transmitted through tissue is used to compute the amount of  
30 oxygen saturation in the arterial blood. Both of these methods are useful for measuring, for example, the oxygen

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saturation in blood but cannot be readily utilized for measuring the concentration of glucose or other low concentration substances in blood. The reasons are related to the fact that the optical absorption spectra of oxyhemoglobin, which corresponds to fully oxygenated blood, and deoxyhemoglobin, which corresponds to fully deoxygenated blood, are significantly different from each other. Furthermore, the optical absorption spectra of blood in the 660 to 9660 nm region of the spectrum is significantly stronger than the background optical absorption of the blood-less tissue. Lastly, the relative concentration of hemoglobin is normally about 150 times higher than that of glucose and hemoglobin has a much higher optical absorption compared to that of glucose.

#### 15 Summary of the Invention

The present invention is based on information derived from the continuous differential spectra of blood obtained noninvasively through the skin by illuminating the tissue with light which rapidly varies in frequency over time.

20 This differential optical spectra (absorption vs. wavelength) is obtained by measuring the difference between the total attenuation of tissue containing a first volume of blood and the same tissue containing a second volume of blood, which is an incremental or a decremental change from the first volume of the blood. Information related to the content of glucose in the blood is then derived from analyzing the features of this differential spectra over a selected range of wavelengths.

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Brief Description of the Drawings

Figure 1 is a normalized plot of a typical optical spectrum (absorption vs. wavelength) of tissue containing blood.

5 Figure 2 is a normalized plot of a optical absorption spectrum of water.

Figure 3 is a block diagram of an apparatus for determining blood analyte concentration in vivo using differential spectrum analysis.

10 Figure 4A are two optical absorption spectra of tissue taken from the same tissue site for two different volumes of blood.

Figure 4B is a normalized differential optical absorption spectrum corresponding to the spectra shown in  
15 Fig. 4A.

Fig. 5 is a block diagram showing an alternate embodiment of Fig. 3.

Fig. 6 is a plot of glucose absorption versus time during the normal cardiac cycle.

20 Detailed Description of the Drawings

The spectrum shown in Fig. 1 represents a typical optical transmission spectrum of tissue containing blood acquired by a spectrophotometer in the wavelength region between 600 nm in the visible and 2500 nm in the infrared.

25 The basic shape and relative magnitude of the absorption peaks in this spectra are similar to that of water (as shown for comparison in Fig. 2) which is known to be the major optical interfering constituent in blood and tissues for in vivo infrared spectroscopy. If the concentration of  
30 glucose in the blood is changed within physiological ranges

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compatible with life, the basic features of the spectra shown in Fig. 1 will remain unchanged, namely, the difference between the two spectra is so minute that it cannot be detected with ordinary spectrophotometers  
5 equipped with photodetectors sensitive to radiation in the corresponding infrared region. The main reason for that is the intrinsically high optical absorption of water compared to glucose and the relatively smaller concentration of glucose compared to that of water in blood and living  
10 tissue. In practical terms, in order to be able to detect variations in the optical absorption spectra of living tissue as a result of changes in the concentration of glucose in that tissue, it is essential to use an optical detector which can discriminate between changes in light  
15 intensities amounting to levels well below the intrinsic noise level of the optical detector itself. With the present state of the technology, this is impractical to accomplish. The present invention overcomes this problem by generating a differential spectrum which contains  
20 information that is significantly more sensitive to physiological variations in the level of blood glucose.

Fig. 3 illustrates how this differential spectra is generated. A light source 10, for example a quartz halogen lamp, powered by a power supply 12 is used to generate  
25 light in the wavelength region of interest. The light generated by the lamp is focused by optical lenses 14 onto optically tuneable filter 18. Alternatively, a narrow range of wavelengths can be pre-selected by passing the beam through an appropriate optical filter 16. The  
30 variable optical filter 18 is powered by an electronic driver 38. Filter 18 is used to select a certain



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wavelength and intensity beam of light 19 at its output. Preferably filter 18 comprises an acousto-optical tunable filter (AOTF) which is a solid-state tunable band-pass optical filter that allows very fast (fractions of a second, or less) narrow wavelength scanning. Other means of generating a fast scanning monochromatic light beam can also be used, instead.

The light 19 is divided by beam splitter 20 into two beams A and B. Beam B is reflected by mirror 22 and enters body tissue 24 at a site adjacent to the entry point of beam A.

The blood volume at the site of entry of beam A is greater than at entry of beam B. Modulation of the blood volume at the adjacent sites may be accomplished in a number of ways. In Fig. 3 a suitable tissue site such as an ear lobe or hand web is used and a light transparent clamp 26 is applied to the entry site of beam B to compress the tissue at that location. Similar light beams A and B enter the tissue 24 and after being partially absorbed by the tissue emerge as light beams A' and B'. Beams A' and B' are reflected by mirrors 28 and 30 onto a single photodetector and preamplifier 32 to produce an electrical signal corresponding to the differential spectra of the two adjacent tissue sites; therefore representing the differential absorptive spectra of blood.

This differential spectra is illustrated in Fig. 4B which shows the results of subtracting the absorptive spectra of beam A passing through the site with greater blood volume (Curve A of Fig. 4A) with the absorptive spectra of beam B passing through the lesser volume site (Curve B of Fig. 4A).

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The driver 38 consists of a high frequency oscillator and power amplifier and is also used to chop the light propagating through the tuneable filter such that the output 19 is a train of optical pulses with a predetermined duty cycle, frequency, wavelength and intensity. The output of the photodetector/preamplifier 32 is further amplified by a sensitive amplifier 34 which can be a lock-in amplifier. If a lock-in amplifier is used, a reference signal taken from the driver 38 is used to synchronize the AOTF (18) with the lock-in amplifier. The output from this amplifier 39 is acquired by a computer 36 which is used to process the data and derive the information related to the concentration of the unknown analyte for presentation by a read-out meter 40.

The spectra shown in Fig. 4B represent the differential spectra of tissue generated by modulating the amount of blood in the tissue. Therefore, the shape of this spectra is characteristic of the spectra of blood. Since blood contains many biochemical analytes in addition to glucose, the spectra shown in Fig. 4B is a composite broad spectra and it contains information relative to the concentration of many blood analytes, including glucose. Some wavelength ranges (for example, 1580 to 1640 nm) contain information predominantly characteristic of blood glucose whereas other wavelengths (for example 1700-1750 nm) convey information predominantly related to other blood analytes, such as lipids. In order to derive information on blood glucose concentration, the spectra in Fig. 4B must be processed in a computer 36 using a number of different mathematical algorithms utilizing, for example, various known multivariate calibration techniques (see, for

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example, the book by H. Martens and T. Naes entitled "Multivariate Calibration", published by John Wiley and Sons, New York, 1989) such as: Partial Least-Squares (e.g., see paper by H. Michael Heise, Ralf Marbach, et al.,

5 "Multivariate Determination of Glucose in Whole Blood by Attenuated Total Reflection Infrared Spectroscopy" in Analytical Chemistry, Vol. 61, No. 18, September 15, pp. 2009-2015, 1989), Principal Component Regression (e.g., see paper by R. Marbach and H.M. Heise, "Calibration Modeling

10 by Partial Least-Squares and Principal Component Regression and its Optimization Using an Improved Leverage Correction for Prediction Testing" in Chemometrics and Intelligent Laboratory Systems, Vol. 9, pp. 45-63, 1990), special Fourier filtering procedures (e.g., see paper by Mark A.

15 Arnold and Gary W. Small, "Determination of Physiological Levels of Glucose in an Aqueous Matrix with Digitally Filtered Fourier Transform Near-Infrared Spectra", Analytical Chemistry, Vol. 62, pp. 1456-1464, 1990), neural networks (e.g., see paper by Peter A. Jansson, "Neural

20 Networks: An Overview" in Analytical Chemistry, Vol. 63, No. 6, March 15, pp. 357A-362A, 1991), etc. The resultant determination may then be presented in various forms on display 40.

The optical detection system described above has the

25 ability to instantaneously frequency scan a tissue containing two different blood volumes such that the physiological and biochemical variables in the tissue remain virtually the same between consecutive scans. Conventional optical scanning devices, such as diffracting

30 gratings or a mechanical device which consists of multiple band-pass interference filters mounted parallel to the

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incident light beam or tilted at different angles with respect to the incident beams, are not suitable for this application because they are too slow and the poor wavelength reproducibility of these mechanical devices is a major limiting factor when trying to measure small changes in the optical absorption spectra of the tissue. The unique properties of the electronic AOTF are utilized in this invention to generate a differential spectra from a living tissue which is similar to the intrinsic optical absorption property of blood.

Another embodiment of this invention is shown in Fig. 5. According to this arrangement, a single tissue site 24' is illuminated by a single beam A'' generated, for example, by an AOTF device 18'. The blood content in this tissue is changed by rapidly applying an external pressure on the tissue using for instance a light transparent electro-mechanically squeezing head or clamp 26'. The properties of this head is such that it allows light to be transmitted through the tissue and it can be used to change the thickness of the tissue simultaneously during the measurement. Since the AOTF is capable of switching wavelengths at extremely high rates, it is possible to apply a quick external pressure pulse to squeeze out some of the blood in the tissue without causing any damage to the tissue or without altering the biochemical status of the tissue and take two successive scans of the tissue. One scan  $A_{pp}$  is obtained before the external pressure pulse is applied to the tissue and the second scan  $A_{pp}$  is obtained immediately after the external pressure pulse is removed. The two scans are then subtracted from each other

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in detector/preamplifier unit 32' to provide the differential spectra, which is further amplified by amplifier 34, as shown in Fig. 3. This procedure can be repeated several times in a periodic manner in order to  
5 acquire multiple scans which can then be averaged in time to improve the overall signal-to-noise ratio of the measurement.

Alternatively, as shown in the typical photoplethysmogram of Fig. 6, the same procedure can be  
10 utilized without the external application of pressure by relying on the presence of the natural blood pressure pulse 1 to modulate the amount of blood in the tissue. The block diagram shown in Fig. 5 is suitable for performing this measurement, except that the electro-mechanically squeezing  
15 clamp 26' is not required. Accordingly, a fast wavelength scan between 1100 nm and 2500 nm is first obtained during the peak diastolic phase of the blood pressure pulse point #2 and then the same wavelength scan is repeated during the peak systolic period of the blood pressure point # 3, as  
20 illustrated in Fig. 6. These two scans do not need to be synchronized with the peak and valley of the blood pressure waveform 1 but can occur at different times in the cardiac cycle, for example, points 4 and 5, or points 6 and 7, provided the two consecutive wavelength scans occur when  
25 different amounts of blood are present inside the tissue.

As shown in Fig. 6, a separate absorption versus wavelength spectrum is generated each time there is a change in the volume of blood in the tissue. The difference between these spectra will have features similar  
30 to that depicted in Fig. 4B. Absolute calibration of the measurement is obtained by numerically correlating the

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features of this differential absorption spectra, shown, for example, in Fig. 4B with different concentrations of glucose during an empirical calibration study in patients or volunteers undergoing standard glucose tolerance tests.

- 5 These spectral features consist of local peaks and valleys corresponding to regions in the spectra where various blood analytes absorb the optical radiation by different amounts.

The present invention overcomes the deficiencies in the prior art in several ways. Firstly, it provides a  
10 simple way to obtain absolute spectral data from blood by eliminated or canceling out the major optical interference caused by the skin and other non-blood components in the tissues. This makes the measurement significantly more accurate and repeatable since the optical properties of  
15 blood are similar among different individuals whereas the optical properties of skin and blood-less tissues are unpredictable and can vary widely among different subjects. Secondly, it allows significantly higher measurement sensitivity for physiological variations in the  
20 concentration of glucose and other analytes in blood. Thirdly, it provides a method for absolute calibration of the measurement.

Although the method described in this invention relates to the measurement of glucose in blood, it should  
25 be understood that the same technique is also applicable for measurement of other low concentration biochemical analytes in blood such a urea, alcohol, cholesterol, and various other important blood constituents of clinical relevance.

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CLAIMS

1. A non-invasive method for measuring the concentration of analyte in living tissue comprising the steps of:
  - 5 a) illuminating the tissue with a first light beam varying in frequency over a first time period;
  - b) detecting the first light beam after the beam has traversed a first blood volume of tissue containing said analyte to produce a first absorption spectra;
  - 10 c) changing the blood volume of tissue;
  - d) illuminating the changed blood volume of tissue with a second light beam which varies in frequency over a second time period;
  - 15 e) detecting the second light beam after the beam has traversed a second blood volume of tissue containing said analyte to produce a second absorption spectra;
  - f) combining the two absorption spectra to produce a differential absorption spectra.
- 20 2. The method of Claim 1 wherein the differential spectra is processed to determine analyte concentration.
3. The method of Claim 2 wherein the analyte is glucose.
4. The method of Claim 2 wherein the light is detected by a photodetector and the absorption spectra comprises  
25 an electrical signal.

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5. The method of Claim 1 wherein the frequency is varied between 1100 nanometers and 2500 nanometers.
6. The method of Claim 1 wherein the blood volume is changed electromechanically.
- 5 7. The method of Claim 1 wherein the blood volume is changed by the natural blood pressure pulse of the cardiac cycle.
8. A non-invasive method for measuring the concentration of analyte in living tissue comprising the steps of:
  - 10 a) illuminating the tissue with a first light beam varying in frequency over a first time period;
  - b) rapidly changing the blood volume of the tissue from a first volume to a second volume;
  - c) detecting the first light beam after the beam has traversed a first volume of tissue containing  
15 said analyte to produce a first absorption spectra;
  - d) detecting the second light beam after the beam has traversed a second volume of tissue  
20 containing said analyte to produce a second absorption spectra;
  - e) combining the two absorption spectra to produce a differential absorption spectra.
9. The method of Claim 8 wherein the differential spectra  
25 is processed to determine analyte concentration.
10. The method of Claim 8 wherein the analyte is glucose.



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11. Apparatus for non-invasive measurement of the concentration of analyte in living tissue comprising:
- a) a light source for generating a beam of light;
  - b) a tuner for varying the frequency of said beam of light;
  - c) a photosensitive detector for detecting said frequency varying light after traversing said tissue:
    - (i) when the tissue contains a first volume of blood; and
    - (ii) when the tissue contains a second volume of blood; and
  - d) generating means for generating a differential signal proportional to the difference between the light detected versus frequency for each signal detected in (c)(i) and (ii) above.
12. The apparatus of Claim 11 wherein the tuner comprises an acousto-optical tunable filter.
13. The apparatus of Claim 11 including a beam splitter for dividing the frequency varied light beam into two beams, one of which traverses a greater volume of blood than the other.
14. The apparatus of Claim 11 including clamp means for varying the volume of blood in the tissue traversed by the light.

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15. The apparatus of Claim 14 wherein the clamp means is an optically transparent body.

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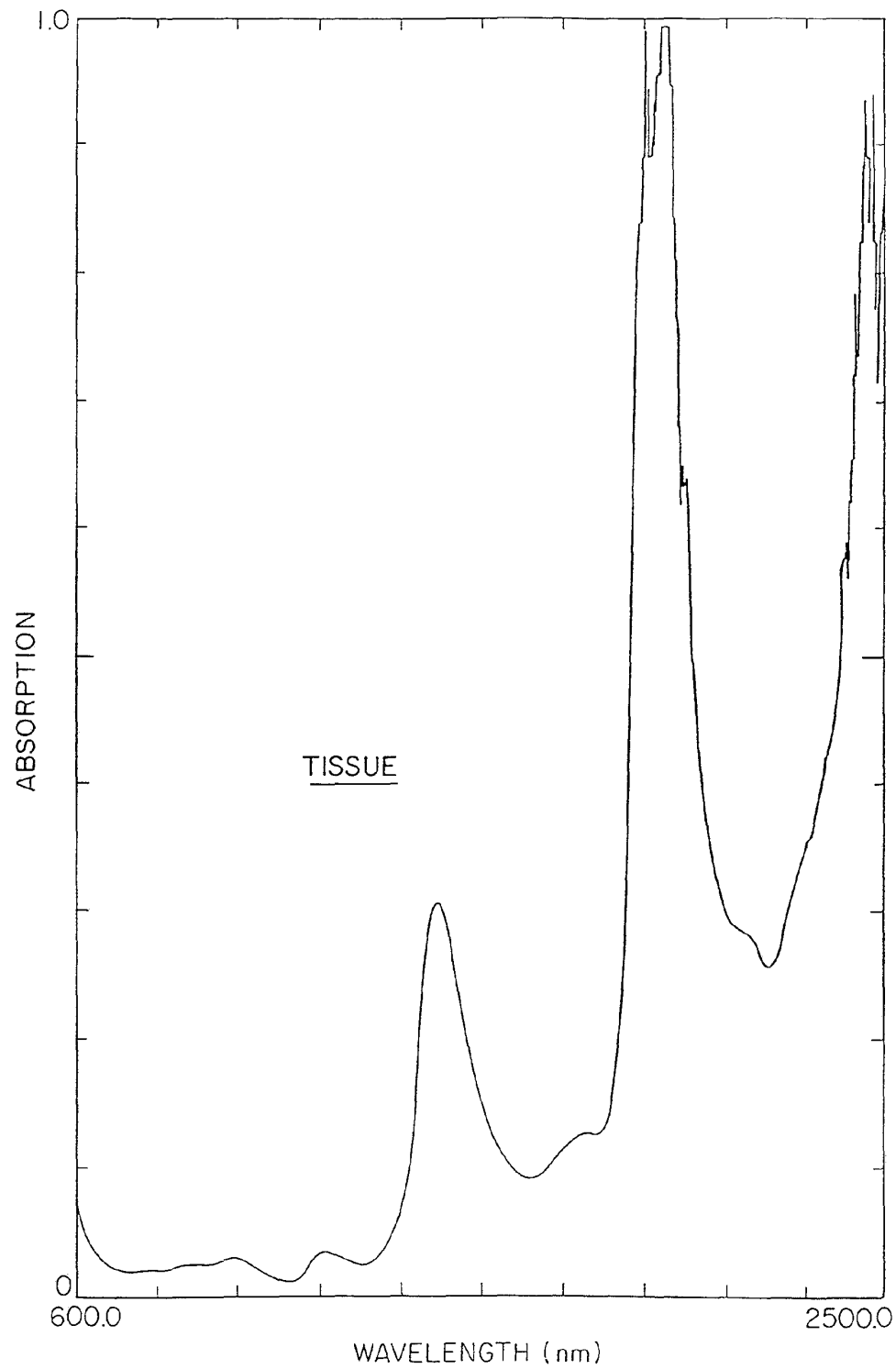


Fig. 1

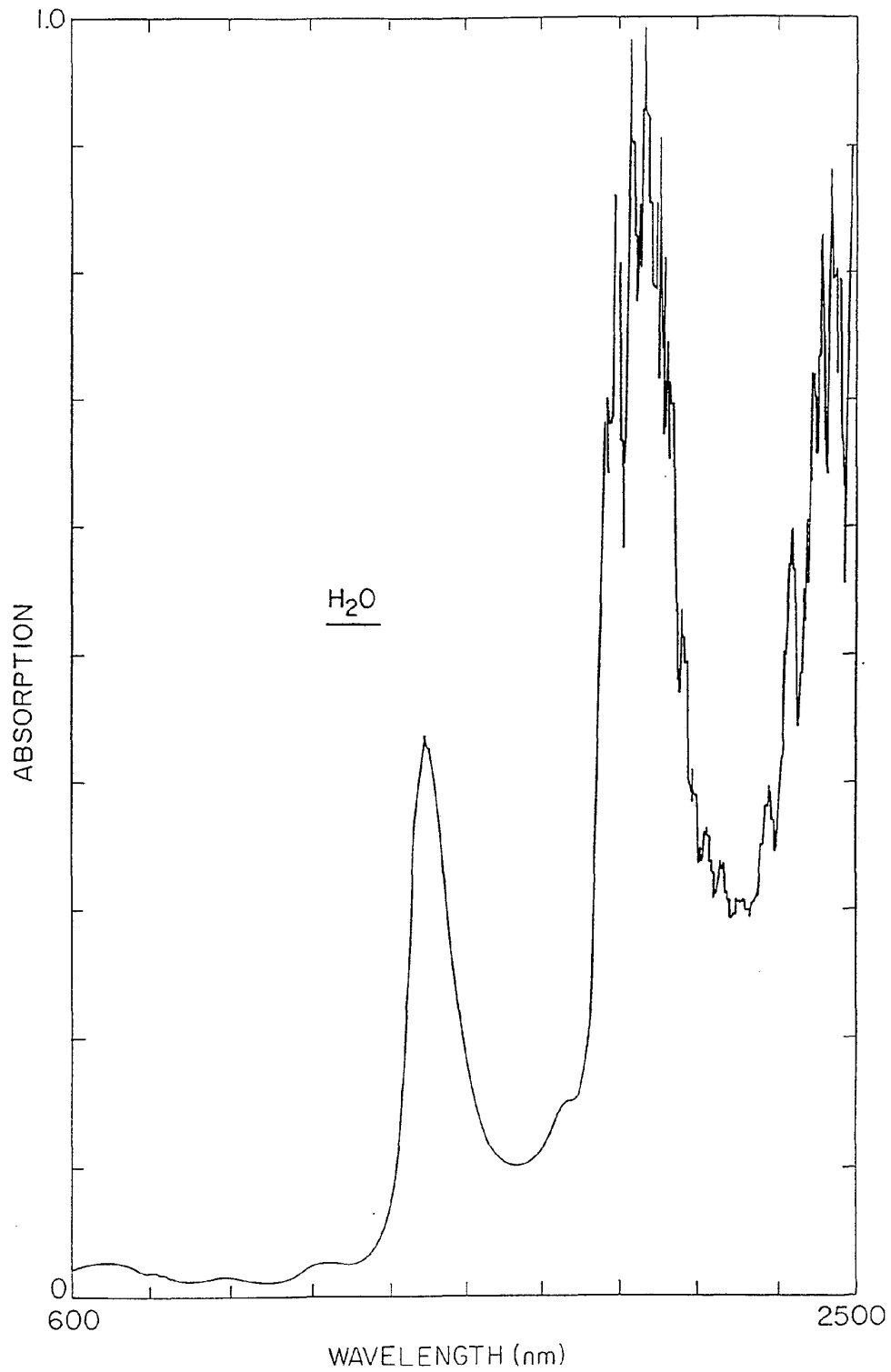
Page 422 of 614

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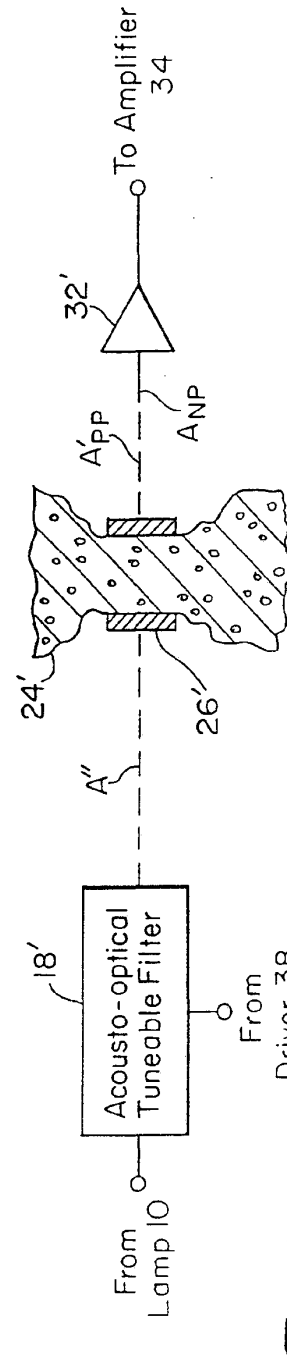
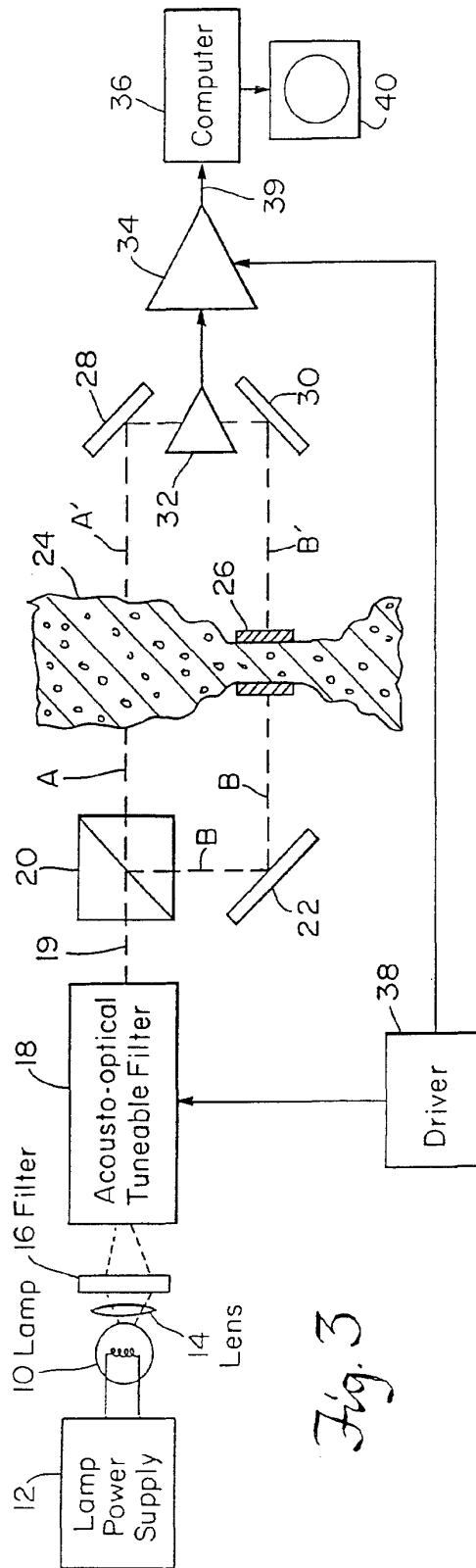
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*Fig. 2*

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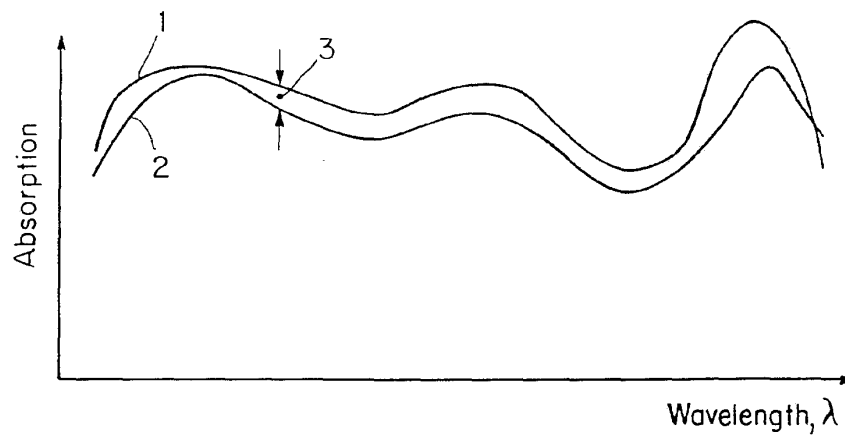


Fig. 4A

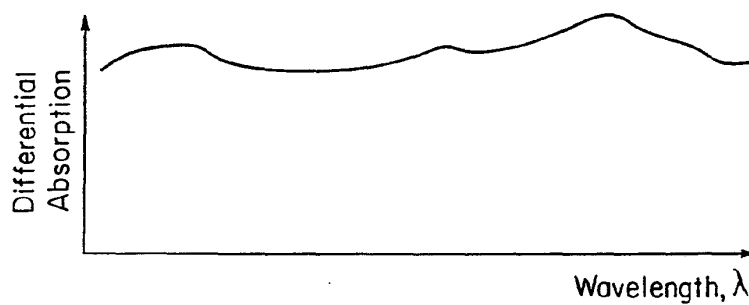


Fig. 4B

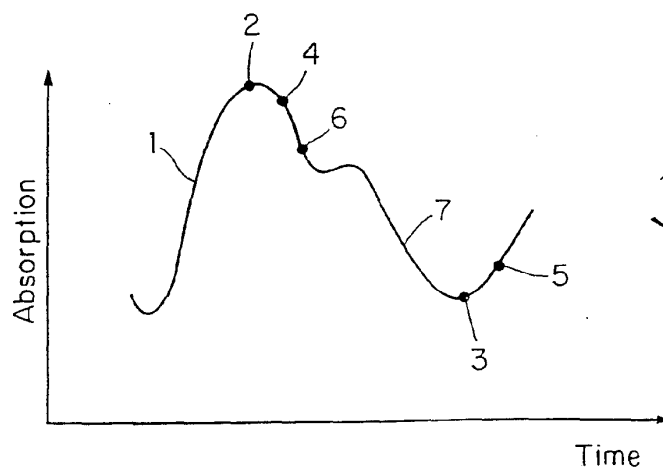


Fig. 6

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## INTERNATIONAL SEARCH REPORT

PCT/US 92/01330

International Application No

<b>I. CLASSIFICATION OF SUBJECT MATTER</b> (if several classification symbols apply, indicate all) <sup>6</sup>		
According to International Patent Classification (IPC) or to both National Classification and IPC		
Int.Cl. 5 A61B5/00; G01N21/31		
<b>II. FIELDS SEARCHED</b>		
Minimum Documentation Searched <sup>7</sup>		
Classification System	Classification Symbols	
Int.Cl. 5	A61B ; G01N	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched <sup>8</sup>		
<b>III. DOCUMENTS CONSIDERED TO BE RELEVANT<sup>9</sup></b>		
Category <sup>10</sup>	Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup>	Relevant to Claim No. <sup>13</sup>
Y A	US,A,4 655 225 (C. DÄHNE ET AL.) 7 April 1987 see column 4, line 22 - line 24 see column 4, line 47 - column 5, line 10 see column 6, line 3 - line 60 see column 9, line 17 - line 48; figures 1-5 ---	1,8 2-5,9-11
Y A	US,A,4 927 264 (T. SHIGA ET AL.) 22 May 1990 see column 2, line 52 - column 3, line 3  see column 3, line 35 - column 4, line 5; figures ---	1,8 4,6,7, 11,14
A	US,A,4 882 492 (K. J. SCHLAGER) 21 November 1989  see column 2, line 59 - column 3, line 36; figures 1,2 ---	1-5, 8-11,13
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<sup>10</sup> Special categories of cited documents : <sup>"A"</sup> document defining the general state of the art which is not considered to be of particular relevance <sup>"E"</sup> earlier document but published on or after the international filing date <sup>"L"</sup> document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) <sup>"O"</sup> document referring to an oral disclosure, use, exhibition or other means <sup>"P"</sup> document published prior to the international filing date but later than the priority date claimed <sup>"T"</sup> later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention <sup>"X"</sup> document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step <sup>"Y"</sup> document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. <sup>"&amp;"</sup> document member of the same patent family		
<b>IV. CERTIFICATION</b>		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
18 SEPTEMBER 1992	12. 10. 92	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	FONTENAY P.H.	

Form PCT/ISA/210 (second sheet) (January 1985)

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International Application No

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	EP,A,0 404 562 (UNIVERSITY OF NEW MEXICO) 27 December 1990 see claims  ---	

Form PCT/ISA/210 (extra sheet) (January 1985)



**ANNEX TO THE INTERNATIONAL SEARCH REPORT  
ON INTERNATIONAL PATENT APPLICATION NO. US 9201330  
SA 61745**

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.  
The members are as contained in the European Patent Office EDP file on  
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-4655225	07-04-87	None	
US-A-4927264	22-05-90	None	
US-A-4882492	21-11-89	None	
EP-A-0404562	27-12-90	US-A- 4975581	04-12-90
		AU-A- 5771490	03-01-91
		CA-A- 2019511	21-12-90
		JP-A- 3114441	15-05-91

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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Electronic Acknowledgement Receipt	
<b>EFS ID:</b>	7360280
<b>Application Number:</b>	12534827
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	1308
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	20995
<b>Filer:</b>	Jarom D. Kesler/Chelsea Pearsall
<b>Filer Authorized By:</b>	Jarom D. Kesler
<b>Attorney Docket Number:</b>	MLHUM.002A
<b>Receipt Date:</b>	06-APR-2010
<b>Filing Date:</b>	03-AUG-2009
<b>Time Stamp:</b>	18:16:25
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

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**File Listing:**

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Filed (SB/08)	002A.pdf	527706 27eeda73ab1ba712c327555d1a7c36712db5c3a0	no	10

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<b>Information:</b>					
<b>Total Files Size (in bytes):</b>			2053814		
<p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b>  <b>If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</b></p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b>  <b>If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</b></p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b>  <b>If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</b></p>					



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
12/534,827	08/03/2009	Jeroen Poeze	MLHUM.002A

CONFIRMATION NO. 1308

## PUBLICATION NOTICE

20995

KNOBBE MARTENS OLSON & BEAR LLP  
 2040 MAIN STREET  
 FOURTEENTH FLOOR  
 IRVINE, CA 92614



\*OC000000040029622\*

**Title:**MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS

**Publication No.**US-2010-0030040-A1

**Publication Date:**02/04/2010

## NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

The publication may be accessed through the USPTO's publicly available Searchable Databases via the Internet at [www.uspto.gov](http://www.uspto.gov). The direct link to access the publication is currently <http://www.uspto.gov/patft/>.

The publication process established by the Office does not provide for mailing a copy of the publication to applicant. A copy of the publication may be obtained from the Office upon payment of the appropriate fee set forth in 37 CFR 1.19(a)(1). Orders for copies of patent application publications are handled by the USPTO's Office of Public Records. The Office of Public Records can be reached by telephone at (703) 308-9726 or (800) 972-6382, by facsimile at (703) 305-8759, by mail addressed to the United States Patent and Trademark Office, Office of Public Records, Alexandria, VA 22313-1450 or via the Internet.

In addition, information on the status of the application, including the mailing date of Office actions and the dates of receipt of correspondence filed in the Office, may also be accessed via the Internet through the Patent Electronic Business Center at [www.uspto.gov](http://www.uspto.gov) using the public side of the Patent Application Information and Retrieval (PAIR) system. The direct link to access this status information is currently <http://pair.uspto.gov/>. Prior to publication, such status information is confidential and may only be obtained by applicant using the private side of PAIR.

Further assistance in electronically accessing the publication, or about PAIR, is available by calling the Patent Electronic Business Center at 1-866-217-9197.

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101



## UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
12/534,827	08/03/2009	3768	2218	MLHUM.002A	34	3

CONFIRMATION NO. 1308

## UPDATED FILING RECEIPT



\*OC000000038389160\*

20995  
 KNOBBE MARTENS OLSON & BEAR LLP  
 2040 MAIN STREET  
 FOURTEENTH FLOOR  
 IRVINE, CA 92614

Date Mailed: 10/26/2009

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

## Applicant(s)

Jeroen Poeze, Mission Viejo, CA;  
 Marcelo Lamego, Coto De Caza, CA;  
 Sean Merritt, Lake Forest, CA;  
 Cristiano Dalvi, Mission Viejo, CA;  
 Hung Vo, Garden Grove, CA;  
 Johannes Bruinsma, Mission Viejo, CA;  
 Ferdyan Lesmana, Irvine, CA;  
 Massi Joe E. Kiani, Laguna Niguel, CA;

## Assignment For Published Patent Application

MASIMO Laboratories, Inc., Irvine, CA

**Power of Attorney:** The patent practitioners associated with Customer Number 20995

## Domestic Priority data as claimed by applicant

This appln claims benefit of 61/086,060 08/04/2008  
 and claims benefit of 61/086,108 08/04/2008  
 and claims benefit of 61/086,063 08/04/2008  
 and claims benefit of 61/086,057 08/04/2008  
 and claims benefit of 61/091,732 08/25/2008

## Foreign Applications

**If Required, Foreign Filing License Granted:** 08/13/2009

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 12/534,827**

**Projected Publication Date:** 02/04/2010

**Non-Publication Request:** No

**Early Publication Request:** No  
**Title**

MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS

**Preliminary Class**

600

## PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at <http://www.uspto.gov/web/offices/pac/doc/general/index.html>.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, <http://www.stopfakes.gov>. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4158).

**LICENSE FOR FOREIGN FILING UNDER**  
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**Title 37, Code of Federal Regulations, 5.11 & 5.15**

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The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

**NOT GRANTED**

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).



## UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
12/534,827	08/03/2009	Jeroen Poeze	MLHUM.002A

**CONFIRMATION NO. 1308****POA ACCEPTANCE LETTER**

20995

KNOBBE MARTENS OLSON & BEAR LLP  
 2040 MAIN STREET  
 FOURTEENTH FLOOR  
 IRVINE, CA 92614



\*OC000000038389075\*

Date Mailed: 10/26/2009

**NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY**

This is in response to the Power of Attorney filed 10/14/2009.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

/mbayou/

Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101



Docket No.: MLHUM.002A

October 14, 2009

Page 1 of 1

Please Direct All Correspondence to Customer Number 20995

**RESPONSE TO FORMALITIES NOTICE**

Applicant : Jeroen Poeze et al.  
App. No : 12/534,827  
Filed : August 3, 2009  
For : MULTI-STREAM DATA  
COLLECTION SYSTEM FOR  
NONINVASIVE MEASUREMENT OF  
BLOOD CONSTITUENTS  
Art Unit : 3768  
Conf No. : 1308

**CERTIFICATE OF EFS WEB  
TRANSMISSION**

I hereby certify that this correspondence, and any other attachment noted on the automated Acknowledgement Receipt, is being transmitted from within the Pacific Time zone to the Commissioner for Patents via the EFS Web server on:

October 14, 2009

(Date)

Jarom D. Kesler, Reg. No. 57,046

**Mail Stop Missing Parts  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450**

Dear Sir:

The above-captioned application was filed without a Declaration and/or filing fees. Enclosed in compliance with 37 CFR 1.53(f) are the following.

- (X) A Declaration in 3 pages.
- (X) General Power of Attorney, Statement under 37 CFR 3.73(b), and Assignment in 11 pages.
- (X) Supplemental Application Data Sheet in 6 pages.
- (X) Fees will be paid via EFS Web.

The Commissioner is hereby authorized to charge any additional fees which may be required, now or in the future, or credit any overpayment, to Account No. 11-1410.

Jarom D. Kesler  
Registration No. 57,046  
Attorney of Record  
Customer No. 20,995  
(949) 760-0404

7954084  
101409

Docket No.: MLHUM.002A

October 14, 2009

Page 1 of 1

Please Direct All Correspondence to Customer Number 20995

**RESPONSE TO FORMALITIES NOTICE**

Applicant : Jeroen Poeze et al.  
App. No : 12/534,827  
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Jarom D. Kesler  
Registration No. 57,046  
Attorney of Record  
Customer No. 20,995  
(949) 760-0404

7954084  
101409

**DECLARATION FOR UTILITY OR DESIGN APPLICATION  
UNDER 37 CFR 1.63**

Docket No.: MLHUM.002A

Page 1 of 3

Title: MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE  
MEASUREMENT OF BLOOD CONSTITUENTS

Inventors: Poeze, Jeroen; Lamego, Marcelo; Merritt, Sean; Dalvi, Cristiano; Vo, Hung;  
Bruinsma, Johannes; Lesmana, Ferydan; Kiani, Massi Joe E.

Please Direct All Correspondence to Customer Number 20995

This Declaration is directed to the invention that was filed as Application No.  
12/534,827, on August 3, 2009

As a below named inventor:

I believe the inventors named below to be the original and first inventors of the subject  
matter which is described and claimed and for which a patent is sought;


I have reviewed and understand the contents of the above-identified application,  
including the claims, and any amendment filed herewith or identified above;

I acknowledge the duty to disclose information which is material to patentability as  
defined in 37 CFR 1.56;

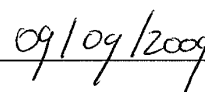
I hereby declare that all statements made herein of my own knowledge are true and that  
all statements made on information and belief are believed to be true; and further that these  
statements were made with the knowledge that willful false statements and the like so made are  
punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States  
Code and that such willful, false statements may jeopardize the validity of the application or any  
patent issued thereon.

Full name of **first** inventor: Jeroen Poeze

Signature:



Date:



Citizenship:

NL

Mailing Address:

21622 Marguerite Parkway #342, Mission Viejo, CA 92692

**DECLARATION FOR UTILITY OR DESIGN APPLICATION  
UNDER 37 CFR 1.63**

Docket No.: MLHUM.002A

Page 2 of 3

Title: MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE  
MEASUREMENT OF BLOOD CONSTITUENTS

Inventors: Poeze, Jeroen; Lamego, Marcelo; Merritt, Sean; Dalvi, Cristiano; Vo, Hung;  
Bruinsma, Johannes; Lesmana, Ferydan; Kiani, Massi Joe E.

Please Direct All Correspondence to Customer Number 20995

Full name of **second** inventor: Marcelo Lamego

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

Citizenship: \_\_\_\_\_

BR

Mailing Address: \_\_\_\_\_

18 Lyra Way, Coto De Caza, CA 92679

Full name of **third** inventor: Sean Merritt

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

Citizenship: \_\_\_\_\_

US

Mailing Address: \_\_\_\_\_

22273 Vista Verde Drive, Lake Forest, CA 92630

Full name of **fourth** inventor: Cristiano Dalvi

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

Citizenship: \_\_\_\_\_

BR

Mailing Address: \_\_\_\_\_

21622 Marguerite Pkwy #6, Mission Viejo, CA 92692

Full name of **fifth** inventor: Hung Vo

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

Citizenship: \_\_\_\_\_

US

Mailing Address: \_\_\_\_\_

8801 Mays Ave, Garden Grove, CA 92844

**DECLARATION FOR UTILITY OR DESIGN APPLICATION  
UNDER 37 CFR 1.63**

Docket No.: MLHUM.002A

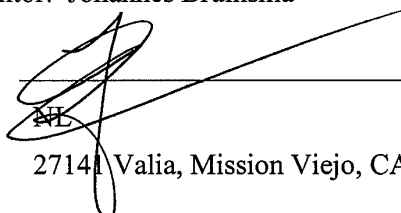
Page 3 of 3

Title: MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE  
MEASUREMENT OF BLOOD CONSTITUENTS

Inventors: Poeze, Jeroen; Lamego, Marcelo; Merritt, Sean; Dalvi, Cristiano; Vo, Hung;  
Bruinsma, Johannes; Lesmana, Ferydan; Kiani, Massi Joe E.

Please Direct All Correspondence to Customer Number 20995

Full name of **sixth** inventor: Johannes Bruinsma

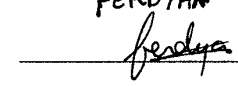
Signature: 

Date: 09/09/09

Citizenship: NL

Mailing Address: 27141 Valia, Mission Viejo, CA 92691

Full name of **seventh** inventor: <sup>F.L.</sup> ~~Ferydan~~ Lesmana  
**FERDYAN**

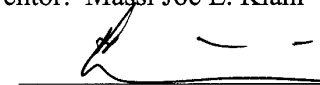
Signature: 

Date: 09/09/2009

Citizenship: ID

Mailing Address: 42 New Season, Irvine, CA 92602

Full name of **eighth** inventor: Massi Joe E. Kiani

Signature: 

Date: 09.09/2009

Citizenship: US

Mailing Address: 35 Brindisi, Laguna Niguel, CA 92677

Send Correspondence To:  
KNOBBE, MARTENS, OLSON & BEAR, LLP  
Customer No. 20995  
7568455

Docket No.: MLHUM.002A

Customer No. 20995

**STATEMENT UNDER 37 CFR § 3.73(b)  
ESTABLISHMENT OF ASSIGNEE**

Applicant : Jeroen Poeze et al.  
App. No. : 12/534,827  
Filed : August 3, 2009  
For : MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE  
MEASUREMENT OF BLOOD CONSTITUENTS  
Examiner : Unknown  
Group Art Unit : 3768

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

This document is being filed with a copy of a Power of Attorney signed by the Assignee. This Statement sets forth the chain of title of the above-identified application.

MASIMO Laboratories, Inc., a corporation, is the Assignee of the entire right, title, and interest of the above-referenced application by virtue of:

The attached copy of the Assignment is being forwarded to the Recordation Branch concurrently under separate cover.

The undersigned is an agent of Customer Number 20995 and is authorized to act on behalf of the Assignee. Please recognize or change the correspondence address for the above-identified application to **Customer No. 20995.**

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: October 14, 2009

By: 

Jarom D. Kesler  
Registration No. 57,046  
Attorney of Record  
Customer No. 20995  
(949) 760-0404

7954118

**PATENT**

Provisional Application No.: 12/534,827  
Filing Date: August 3, 2009

Client Code: MLHUM.002A  
Page 1

**ASSIGNMENT**

WHEREAS, we, JEROEN POEZE a DUTCH citizen, residing at 21622 Marguerite Parkway #342, Mission Viejo, CA 92692, MARCELO LAMEGO a BRAZILIAN citizen, residing at 18 Lyra Way, Coto De Caza, CA 92679, SEAN MERRITT, a US citizen, residing at 22273 Vista Verde Drive, Lake Forest, CA 92630, CRISTIANO DALVI a BRAZILIAN citizen, residing at 21622 Marguerite Pkwy #6, Mission Viejo, CA 92692, HUNG VO a US citizen, residing at 8801 Mays Ave, Garden Grove, CA 92844, JOHANNES BRUINSMA a DUTCH citizen, residing at 27141 Valia, Mission Viejo, CA 92691, FERDYAN LESMANA an INDONESIAN citizen, residing at 42 New Season, Irvine, CA 92602, and MASSI JOE E. KIANI, a US citizen, residing at 35 Brindisi, Laguna Niguel, CA 92677, have invented certain new and useful improvements in a MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS for which we have filed an application for Letters Patent in the United States, Application No. 12/534,827, filed August 3, 2009;

AND WHEREAS, MASIMO LABORATORIES, INC. (hereinafter "ASSIGNEE"), a Delaware Corporation, with its principal place of business at 30 Fairbanks, Suite 100, Irvine, CA 92618, desires to acquire a 100% right, title, and interest in and to said improvements and said Application:

NOW, THEREFORE, in consideration of the sum of One Dollar (\$1.00) to me in hand paid, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, said inventor, do hereby acknowledge that we have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over, unto said ASSIGNEE, its successors, legal representatives and assigns, the entire right, title, and interest throughout the world in, to and under said improvements, and said application including all provisional applications relating thereto (including but not limited to U.S. Provisional Application No(s). 61/086,060, filed August 4, 2008; 61/086,108, filed August 4, 2008; 61/086,063, filed August 4, 2008; 61/086,057, filed August 4, 2008; 61/091,732, filed August 25, 2008), and all divisions, renewals and continuations thereof, and all Letters Patent of the United States which may be granted thereon and all reissues and extensions thereof, and all rights of priority under International Conventions and applications for Letters Patent which may hereafter be filed for said improvements in any country or countries foreign to the United States, and all Letters Patent which may be granted for said improvements in any country or countries foreign to the United States and all extensions, renewals and reissues thereof; and I hereby authorize and request the Commissioner of Patents of the United States, and any Official of any country or countries foreign to the United States, whose duty it is to issue patents on applications as aforesaid, to issue all Letters Patent for said improvements to said ASSIGNEE, its successors, legal representatives and assigns, in accordance with the terms of this instrument.

AND WE DO HEREBY sell, assign, transfer, and convey to ASSIGNEE, his successors, legal representatives, and assigns all claims for damages and all remedies arising out of any

**PATENT**

Provisional Application No.: 12/534,827  
 Filing Date: August 3, 2009

Client Code: MLHUM.002A  
 Page 2

violation of the rights assigned hereby that may have accrued prior to the date of assignment to ASSIGNEE, or may accrue hereafter, including, but not limited to, the right to sue for, collect, and retain damages for past infringements of the said Letters Patent, before or after issuance.

AND WE HEREBY covenant and agree that we will communicate to the ASSIGNEE, successors, legal representatives and assigns, any facts known to me respecting said improvements, and testify in any legal proceeding, assist in the preparation of any other provisional or non-provisional applications relating to the improvements, sign all lawful papers, execute and make all rightful oaths and/or declarations in connection with the Application including any improvements made thereto, any utility (non-provisional) application(s) filed therefrom, and any continuing application(s) filed from aforementioned utility application(s), and generally do everything possible to aid the ASSIGNEE, successors, legal representatives and assigns, to obtain and enforce proper patent protection for said improvements in all countries.

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 09 day of September, 2009.

  
 JEROEN POEZE

STATE OF California }  
 COUNTY OF Orange } ss.

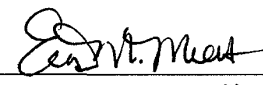
On 09 SEP 2009, before me, Elisa M. Mulet, notary public, personally appeared JEROEN POEZE who proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/are subscribed to the within instrument, and acknowledged to me that HE executed the same in HIS authorized capacity(ies), and that by HIS signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the foregoing paragraph is true and correct.

WITNESS my hand and official seal.

[SEAL]

Notary

  
 Signature



Page 443 of 614

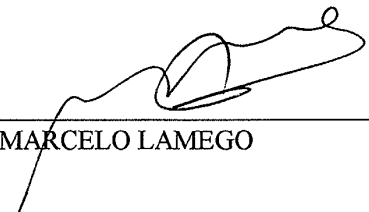
**Appx58107**



Provisional Application No.: 12/534,827  
Filing Date: August 3, 2009

**PATENT**  
Client Code: MLHUM.002A  
Page 3

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 9th day of  
Sept., 2009

  
MARCELO LAMEGO

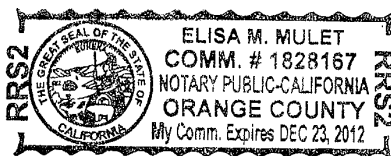
STATE OF California }  
COUNTY OF Orange } ss.

On 09 SEP 2009, before me, Elisa M. Mulet, notary public,  
personally appeared MARCELO LAMEGO who proved to me on the basis of satisfactory  
evidence to be the person(s) whose name(s) is/are subscribed to the within instrument, and  
acknowledged to me that HE executed the same in HIS authorized capacity(ies), and that by HIS  
signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s)  
acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the  
foregoing paragraph is true and correct.

WITNESS my hand and official seal.

[SEAL]



  
Notary Signature

Provisional Application No.: 12/534,827  
Filing Date: August 3, 2009

**PATENT**  
Client Code: MLHUM.002A  
Page 4

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 9 day of  
September, 2009

[Signature]  
SEAN MERRITT

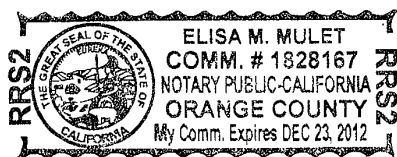
STATE OF California }  
COUNTY OF Orange } ss.

On 09 SEP 2009, before me, Elisa M. Mulet, notary public,  
personally appeared SEAN MERRITT who proved to me on the basis of satisfactory evidence to  
be the person(s) whose name(s) is/are subscribed to the within instrument, and acknowledged to  
me that HE executed the same in HIS authorized capacity(ies), and that by HIS signature(s) on  
the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed the  
instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the  
foregoing paragraph is true and correct.

WITNESS my hand and official seal.

[SEAL]



[Signature]  
Notary Signature

Provisional Application No.: 12/534,827  
Filing Date: August 3, 2009

**PATENT**  
Client Code: MLHUM.002A  
Page 5

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 09 day of  
SEPTEMBER, 2009



CRISTIANO DALVI

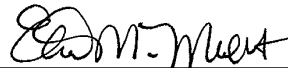
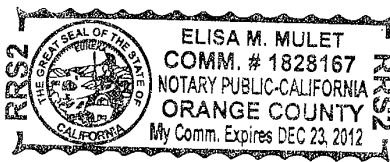
STATE OF California }  
COUNTY OF Orange } ss.

On 09 SEP 2009, before me, Elisa M. Mulet, notary public,  
personally appeared CRISTIANO DALVI who proved to me on the basis of satisfactory evidence  
to be the person(s) whose name(s) is/are subscribed to the within instrument, and acknowledged  
to me that HE executed the same in HIS authorized capacity(ies), and that by HIS signature(s) on  
the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed the  
instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the  
foregoing paragraph is true and correct.

WITNESS my hand and official seal.

[SEAL]




Notary Signature

Provisional Application No.: 12/534,827  
Filing Date: August 3, 2009

**PATENT**  
Client Code: MLHUM.002A  
Page 6

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 09 day of September 2009

  
HUNG VO

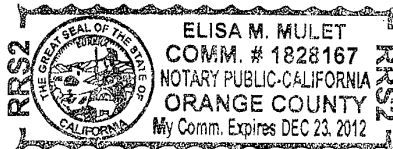
STATE OF California }  
COUNTY OF Orange } ss.

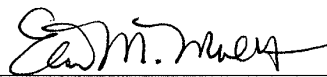
On 09 SEP 2009, before me, Elisa M. Mulet, notary public, personally appeared HUNG VO who proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/are subscribed to the within instrument, and acknowledged to me that HE executed the same in HIS authorized capacity(ies), and that by HIS signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the foregoing paragraph is true and correct.

WITNESS my hand and official seal.

[SEAL]

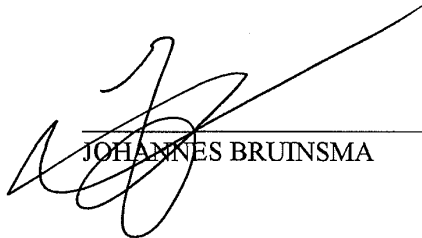


  
Notary Signature

Provisional Application No.: 12/534,827  
Filing Date: August 3, 2009

**PATENT**  
Client Code: MLHUM.002A  
Page 7

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 09 day of September, 2009.

  
JOHANNES BRUINSMA

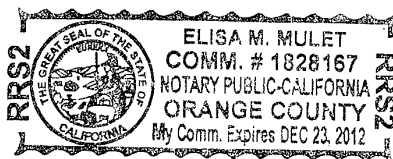
STATE OF California }  
COUNTY OF Orange } ss.

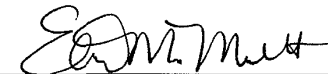
On 09 SEP 2009, before me, Elisa M. Mulet, notary public, personally appeared JOHANNES BRUINSMA who proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/are subscribed to the within instrument, and acknowledged to me that HE executed the same in HIS authorized capacity(ies), and that by HIS signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the foregoing paragraph is true and correct.

WITNESS my hand and official seal.

[SEAL]



  
Notary Signature

Provisional Application No.: 12/534,827  
Filing Date: August 3, 2009

**PATENT**  
Client Code: MLHUM.002A  
Page 8

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 09 day of September, 2009

*Ferdya*  
FERDYAN LESMANA

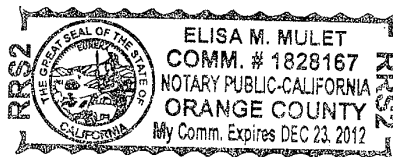
STATE OF California }  
COUNTY OF Orange } ss.

On 09SEP2009, before me, Elisa M. Mulet, notary public, personally appeared FERDYAN LESMANA who proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/are subscribed to the within instrument, and acknowledged to me that HE executed the same in HIS authorized capacity(ies), and that by HIS signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the foregoing paragraph is true and correct.

WITNESS my hand and official seal.

[SEAL]




*Elisa M. Mulet*  
Notary Signature

Provisional Application No.: 12/534,827  
Filing Date: August 3, 2009

**PATENT**  
Client Code: MLHUM.002A  
Page 9

IN TESTIMONY WHEREOF, I hereunto set my hand and seal this 15<sup>th</sup> day of September, 2009.

  
\_\_\_\_\_  
MASSI JOE E. KIANI

STATE OF California }  
COUNTY OF Orange } ss.

On 09/15/2009, before me, Marnelle Ross, notary public, personally appeared MASSI JOE E. KIANI who proved to me on the basis of satisfactory evidence to be the person(s) whose name(s) is/are subscribed to the within instrument, and acknowledged to me that executed the same in authorized capacity(ies), and that by signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed the instrument.

I certify under PENALTY OF PERJURY under the laws of the State of California that the foregoing paragraph is true and correct.

WITNESS my hand and official seal.

[SEAL]

  
\_\_\_\_\_  
Signature



7569054

Docket No.: MASIMO.000GEN

Customer No. 20,995

**REVOCATION  
AND  
GENERAL POWER OF ATTORNEY**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

The undersigned is an empowered representative of the Assignee and hereby appoints the registrants of Knobbe, Martens, Olson & Bear, LLP, **Customer No. 20,995**, as attorneys and agents to represent the Assignee before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned to the Assignee according to the USPTO assignment records or assignment documents supplied with an accompanying Statement Under 37 CFR § 3.73(b). This appointment is to be to the exclusion of the inventor(s) and his attorney(s) in accordance with the provisions of 37 CFR § 3.71.

All previous powers of attorney for the below named Assignee are hereby revoked.

A Statement Under 37 CFR § 3.73(b), signed by a registrant of Knobbe, Martens, Olson & Bear, LLP, is attached setting forth a full chain of title for the subject application owned by the Assignee named below.

Please recognize or change the correspondence address for the above-identified application to **Customer No. 20,995**.

By:

Name:  Chris Kilpatrick

Date:

8/5/04

Title: V.P. Business Development  
and General Counsel

Assignee: MASIMO CORPORATION

Address: 40 Parker, Irvine, CA 92618

H:\DOCS\JMG\JMG-6377.DOC  
072804



**SUPPLEMENTAL APPLICATION DATA SHEET****Application Information**

Application Number:: 12/534,827  
 Filing Date:: August 3, 2009  
 Application Type:: Nonprovisional  
 Subject Matter:: Utility  
 Suggested Group Art Unit:: 3768  
 Title:: MULTI-STREAM DATA COLLECTION SYSTEM FOR  
 NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS  
 Attorney Docket Number:: MLHUM.002A  
 Request for Early Publication?: No  
 Request for Non-Publication?: No  
 Total Drawing Sheets:: 65  
 Small Entity?: No

**Inventor Information 1**

Applicant Authority Type:: Inventor  
 Primary Citizenship Country:: ~~US~~ NL  
 Given Name:: Massi Jeroen  
 Middle Name:: Joe-E-  
 Family Name:: Kiani Poeze  
 City of Residence:: ~~Laguna Niguel~~ Mission Viejo  
 State or Prov. of Residence:: CA  
 Country of Residence:: US  
 Street:: ~~35 Brindisi~~ 21622 Marguerite Parkway #342  
 City:: ~~Laguna Niguel~~ Mission Viejo  
 State or Province:: CA  
 Country:: US

1 Supplemental 12/534,827 August 3, 2009 10/14/09

Docket Number: MLHUM.002A

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Postal or Zip Code:: ~~92677~~ 92692

**Inventor Information 2**

Applicant Authority Type:: Inventor  
Primary Citizenship Country:: BR  
Given Name:: Marcelo  
Family Name:: Lamego  
City of Residence:: Coto De Caza  
State or Prov. of Residence:: CA  
Country of Residence:: US  
Street:: 18 Lyra Way  
City:: Coto De Caza  
State or Province:: CA  
Country:: US  
Postal or Zip Code:: 92679

**Inventor Information 3**

Applicant Authority Type:: Inventor  
Primary Citizenship Country:: US  
Given Name:: Sean  
Family Name:: Merritt  
City of Residence:: Lake\_Forest  
State or Prov. of Residence:: CA  
Country of Residence:: US  
Street:: 22273 Vista Verde Drive  
City:: Lake Forest  
State or Province:: CA

2

Supplemental 12/534,827 August 3, 200910/14/09

Docket Number: MLHUM.002A

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Country:: US  
Postal or Zip Code:: 92630

**Inventor Information 4**

Applicant Authority Type:: Inventor  
Primary Citizenship Country:: BR  
Given Name:: Cristiano  
Family Name:: Dalvi  
City of Residence:: Mission Viejo  
State or Prov. of Residence:: CA  
Country of Residence:: US  
Street:: 21622 Marguerite Pkwy #6  
City:: Mission Viejo  
State or Province:: CA  
Country:: US  
Postal or Zip Code:: 92692

**Inventor Information 5**

Applicant Authority Type:: Inventor  
Primary Citizenship Country:: US  
Given Name:: Hung  
Family Name:: Vo  
City of Residence:: Garden Grove  
State or Prov. of Residence:: CA  
Country of Residence:: US  
Street:: 8801 Mays Ave.  
City:: Garden Grove

Docket Number: MLHUM.002A

State or Province:: CA  
Country:: US  
Postal or Zip Code:: 92844

**Inventor Information 6**

Applicant Authority Type:: Inventor  
Primary Citizenship Country:: NL  
Given Name:: Johannes  
Family Name:: Bruinsma  
City of Residence:: Mission Viejo  
State or Prov. of Residence:: CA  
Country of Residence:: US  
Street:: 27141 Valia  
City:: Mission Viejo  
State or Province:: CA  
Country:: US  
Postal or Zip Code:: 92691

**Inventor Information 7**

Applicant Authority Type:: Inventor  
Primary Citizenship Country:: NL ID  
Given Name:: Jeroen Ferdyan  
Family Name:: Peeze Lesmana  
City of Residence:: Mission Viejo Irvine  
State or Prov. of Residence:: CA  
Country of Residence:: US  
Street:: 21622 Marguirite Parkway #342 42 New Season  
4 Supplemental 12/534,827 August 3, 200910/14/09

City:: ~~Mission Viejo~~ Irvine  
State or Province:: CA  
Country:: US  
Postal or Zip Code:: ~~92692~~ 92602

#### **Inventor Information 8**

Applicant Authority Type:: Inventor  
Primary Citizenship Country:: ~~ID~~ US  
Given Name:: ~~Ferdyan~~ Massi  
Middle Name:: Joe E.  
Family Name:: ~~Lesmana~~ Kiani  
City of Residence:: ~~Irvine~~ Laguna Niguel  
State or Prov. of Residence:: CA  
Country of Residence:: US  
Street:: ~~42 New Season~~ 35 Brindisi  
City:: ~~Irvine~~ Laguna Niguel  
State or Province:: CA  
Country:: US  
Postal or Zip Code:: ~~92602~~ 92677

#### **Correspondence Information**

Correspondence Customer Number:: 20995  
Phone Number:: (949) 760-0404  
Fax Number:: (949) 760-9502  
E-Mail Address:: efilng@kmob.com

Docket Number: MLHUM.002A

**Representative Information**

Representative Customer Number:: 20995

**Domestic Priority Information**

Application::	Continuity Type::	Parent Application::	Parent Filing Date::
This Application	Non-provisional of	61/086060	2008-08-04
This Application	Non-provisional of	61/086108	2008-08-04
This Application	Non-provisional of	61/086063	2008-08-04
This Application	Non-provisional of	61/086057	2008-08-04
This Application	Non-provisional of	61/091732	2008-08-25

**Assignment Information**Assignee Name:: MASIMO Laboratories, Inc.Street:: 30 Fairbanks, Suite 100City:: IrvineState or Province:: CACountry:: USPostal or Zip Code:: 92618

Dated: October 14, 2009

By: 

Jarom D. Kesler

Registration No. 57,046

Attorney of Record

Customer No. 20995

(949) 760-0404

7953274  
101409

Electronic Patent Application Fee Transmittal				
<b>Application Number:</b>	12534827			
<b>Filing Date:</b>	03-Aug-2009			
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
<b>First Named Inventor/Applicant Name:</b>	Massi Joe E. Kiani			
<b>Filer:</b>	Jarom D. Kesler/Nadin Hamoui			
<b>Attorney Docket Number:</b>	MLHUM.002A			
Filed as Large Entity				
<b>Utility under 35 USC 111(a) Filing Fees</b>				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
<b>Basic Filing:</b>				
Utility application filing	1011	1	330	330
Utility Search Fee	1111	1	540	540
Utility Examination Fee	1311	1	220	220
<b>Pages:</b>				
Utility Appl Size fee per 50 sheets >100	1081	1	270	270
<b>Claims:</b>				
Claims in excess of 20	1202	14	52	728
<b>Miscellaneous-Filing:</b>				

CX-1621

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Late filing fee for oath or declaration	1051	1	130	130
<b>Petition:</b>				
<b>Patent-Appeals-and-Interference:</b>				
<b>Post-Allowance-and-Post-Issuance:</b>				
<b>Extension-of-Time:</b>				
<b>Miscellaneous:</b>				
<b>Total in USD (\$)</b>				<b>2218</b>



CX-1621

<b>Electronic Acknowledgement Receipt</b>	
<b>EFS ID:</b>	6263125
<b>Application Number:</b>	12534827
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	1308
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Massi Joe E. Kiani
<b>Customer Number:</b>	20995
<b>Filer:</b>	Jarom D. Kesler/Valerie Jones
<b>Filer Authorized By:</b>	Jarom D. Kesler
<b>Attorney Docket Number:</b>	MLHUM.002A
<b>Receipt Date:</b>	14-OCT-2009
<b>Filing Date:</b>	03-AUG-2009
<b>Time Stamp:</b>	19:02:28
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	yes
Payment Type	Credit Card
Payment was successfully received in RAM	\$2218
RAM confirmation Number	8250
Deposit Account	111410
Authorized User	KNOBBE MARTENS OLSON AND BEAR
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)</p> <p>Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)</p>	

Page 460 of 614

**Appx58124**

CX-1621

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Applicant Response to Pre-Exam Formalities Notice	transmittal.pdf	48889	no	1
			1b1f82dbfb20e674241a64c45a0a17543ddb1ae8		
Warnings:					
Information:					
2	Oath or Declaration filed	declaration.pdf	138234	no	3
			84bf6906963ece2e176239d65f3968a363ffb2be47		
Warnings:					
Information:					
3		statement.pdf	523761	yes	11
			354c2b312a41448f14b49a9059bc9e933482abfb		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Assignee showing of ownership per 37 CFR 3.73(b).		1	10	
	Power of Attorney		11	11	
Warnings:					
Information:					
4	Application Data Sheet	Suppl.pdf	173456	no	6
			77883bc9f942fc3d38f1cedd220323a9602d46a4		
Warnings:					
Information:					
This is not an USPTO supplied ADS fillable form					
5	Fee Worksheet (PTO-875)	fee-info.pdf	40103	no	2
			2ab6fcff71892421bd8b3411f7c01fe7d3b6d295		
Warnings:					
Information:					
Total Files Size (in bytes):			924443		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
**United States Patent and Trademark Office**  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
12/534,827	08/03/2009	3768	0.00	MLHUM.002A	34	3

CONFIRMATION NO. 1308

20995  
 KNOBBE MARTENS OLSON & BEAR LLP  
 2040 MAIN STREET  
 FOURTEENTH FLOOR  
 IRVINE, CA 92614

## FILING RECEIPT



\*OC000000037346805\*

Date Mailed: 08/19/2009

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

## Applicant(s)

Massi Joe E. Kiani, Laguna Niguel, CA;  
 Marcelo Lamego, Coto De Caza, CA;  
 Sean Merritt, Lake Forest, CA;  
 Cristiano Dalvi, Mission Viejo, CA;  
 Hung Vo, Garden Grove, CA;  
 Johannes Bruinsma, Mission Viejo, CA;  
 Jeroen Poeze, Mission Viejo, CA;  
 Ferdyan Lesmana, Irvine, CA;

Power of Attorney: None

## Domestic Priority data as claimed by applicant

This appln claims benefit of 61/086,060 08/04/2008  
 and claims benefit of 61/086,108 08/04/2008  
 and claims benefit of 61/086,063 08/04/2008  
 and claims benefit of 61/086,057 08/04/2008  
 and claims benefit of 61/091,732 08/25/2008

## Foreign Applications

If Required, Foreign Filing License Granted: 08/13/2009

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 12/534,827**

Projected Publication Date: To Be Determined - pending completion of Missing Parts

Non-Publication Request: No

page 1 of 3

**Early Publication Request:** No  
**Title**

MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS

**Preliminary Class**

600

## PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at <http://www.uspto.gov/web/offices/pac/doc/general/index.html>.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, <http://www.stopfakes.gov>. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4158).

**LICENSE FOR FOREIGN FILING UNDER**  
**Title 35, United States Code, Section 184**  
**Title 37, Code of Federal Regulations, 5.11 & 5.15**

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
12/534,827	08/03/2009	Massi Joe E. Kiani	MLHUM.002A

CONFIRMATION NO. 1308

## FORMALITIES LETTER

20995

KNOBBE MARTENS OLSON & BEAR LLP  
 2040 MAIN STREET  
 FOURTEENTH FLOOR  
 IRVINE, CA 92614



\*OC000000037346806\*

Date Mailed: 08/19/2009

## NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

*Filing Date Granted***Items Required To Avoid Abandonment:**

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The statutory basic filing fee is missing.  
*Applicant must submit \$330 to complete the basic filing fee for a non-small entity. If appropriate, applicant may make a written assertion of entitlement to small entity status and pay the small entity filing fee (37 CFR 1.27).*
- The oath or declaration is missing.  
*A properly signed oath or declaration in compliance with 37 CFR 1.63, identifying the application by the above Application Number and Filing Date, is required.*  
*Note: If a petition under 37 CFR 1.47 is being filed, an oath or declaration in compliance with 37 CFR 1.63 signed by all available joint inventors, or if no inventor is available by a party with sufficient proprietary interest, is required.*

The applicant needs to satisfy supplemental fees problems indicated below.

The required item(s) identified below must be timely submitted to avoid abandonment:

- Additional claim fees of **\$728** as a non-small entity, including any required multiple dependent claim fee, are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due.
- To avoid abandonment, a surcharge (for late submission of filing fee, search fee, examination fee or oath or declaration) as set forth in 37 CFR 1.16(f) of **\$130** for a non-small entity, must be submitted with the missing items identified in this notice.

**SUMMARY OF FEES DUE:**

Total additional fee(s) required for this application is **\$2218** for a non-small entity

- **\$330** Statutory basic filing fee.
- **\$130** Surcharge.
- The application search fee has not been paid. Applicant must submit **\$540** to complete the search fee.

- The application examination fee has not been paid. Applicant must submit **\$220** to complete the examination fee for a non-small entity.
- The specification and drawings submitted electronically contain the equivalent of more than 100 pages. Applicant owes **\$270** for 2 pages in excess of **100** pages for a non-small entity.
- Total additional claim fee(s) for this application is **\$728**
  - **\$728** for **14** total claims over 20.

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Office of Data Management, Application Assistance Unit (571) 272-4000, or (571) 272-4200, or 1-888-786-0101



<b>UTILITY APPLICATION</b>	Attorney Docket No.: MLHUM.002A
	First Named Inventor: MASSI JOE E. KIANI Title: MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>Direct all correspondence to Customer No.: 20995</b>	
Date: August 3, 2009 Page 1	

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

The following enclosures are transmitted herewith to be filed in the patent application of:

Inventor(s):

- |                       |                      |
|-----------------------|----------------------|
| 1. MASSI JOE E. KIANI | 2. MARCELO LAMEGO    |
| 3. SEAN MERRITT       | 4. CRISTIANO DALVI   |
| 5. HUNG VO            | 6. JOHANNES BRUINSMA |
| 7. JEROEN POEZE       | 8. FERDYAN LESMANA   |

**APPLICATION:**

(X) Specification in 71 pages.

(X) Drawings in 65 sheets.

**CONTINUITY INFORMATION:**

Application	Relationship	Parent App. No.	Filing Date	Status
This Application	Non-Provisional of	61/086060	2008-08-04	Pending
This Application	Non-Provisional of	61/086108	2008-08-04	Pending
This Application	Non-Provisional of	61/086063	2008-08-04	Pending
This Application	Non-Provisional of	61/086057	2008-08-04	Pending
This Application	Non-Provisional of	61/091732	2008-08-25	Pending

Reference to prior domestic applications is made in the:

(X) Specification.

(X) Enclosed Application Data Sheet (ADS).

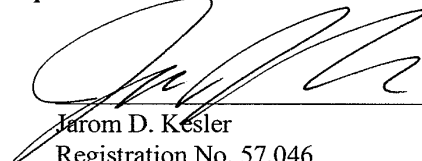
<b>UTILITY APPLICATION</b>	Attorney Docket No.: MLHUM.002A
	First Named Inventor: MASSI JOE E. KIANI
	Title: MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>Direct all correspondence to Customer No.: 20995</b> <span style="float: right;">Date: August 3, 2009 Page 2</span>	

**FILING FEES:**

FEE CALCULATION				
FEE TYPE		FEE CODE	CALCULATION	TOTAL
Basic Utility	1.16(a)(1)	1011 (\$330)		\$330
Search Fee	1.16(k)	1111 (\$540)		\$540
Examination Fee	1.16(o)	1311 (\$220)		\$220
Excess Claims > 20	- 20 =	1202 (\$52)	x 52 =	\$
Independent > 3	- 3 =	1201 (\$220)	x 220 =	\$
Multiple Claim	1.16(j)	1203 (\$390)		\$
Application Size Fee	- 100 =	1081 (\$270) <sup>±</sup>	x 270 =	\$
Recordation Fee	1.21(h)	8021 (\$40)	x 40 =	\$
Non-English Spec.	1.17(i)	1053 (\$130)		\$
<b>TOTAL FEE DUE</b>				<b>\$1,090</b>

<sup>±</sup>Each additional group of 0-50 pages requires this fee. For example, a 101 page application requires this fee once, a 157 page application requires two times this fee, and a 211 page application requires three times this fee.

**(X) The total fees calculated above will be paid at a later date.**

  
 Jarom D. Kesler  
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 Attorney of Record  
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 (949) 760-0404

7577306

CX-1621

Electronic Acknowledgement Receipt	
EFS ID:	5820939
Application Number:	12534827
International Application Number:	
Confirmation Number:	1308
Title of Invention:	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
First Named Inventor/Applicant Name:	Massi Joe E. Kiani
Customer Number:	20995
Filer:	Jarom D. Kesler/Valerie Jones
Filer Authorized By:	Jarom D. Kesler
Attorney Docket Number:	MLHUM.002A
Receipt Date:	03-AUG-2009
Filing Date:	
Time Stamp:	21:50:50
Application Type:	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	no
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**File Listing:**

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		002A.pdf	4349623 a77af3580b4b412aade577a3c990bf188649af0	yes	71

CX-1621

Multipart Description/PDF files in .zip description					
Document Description			Start	End	
Specification			1	66	
Claims			67	70	
Abstract			71	71	
<b>Warnings:</b>					
<b>Information:</b>					
2	Drawings-only black and white line drawings	MLHUM002A.pdf	1408561 a8a858ebcd373015b7007b4faf3040dca1a539e0	no	65
<b>Warnings:</b>					
<b>Information:</b>					
3	Application Data Sheet	M002ADS.pdf	385992 6b9a397e440c31c00b9120a77e45946014eeca9b	no	6
<b>Warnings:</b>					
<b>Information:</b>					
This is not an USPTO supplied ADS fillable form					
4	Transmittal of New Application	M002ATrans.pdf	72186 4105cb11b70e4e34d55086cdfcacba0f98ac48a1	no	2
<b>Warnings:</b>					
<b>Information:</b>					
Total Files Size (in bytes):			6216362		
<p><b>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</b></p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b>  If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b>  If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b>  If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>					

MLHUM.002A

PATENT

**MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE  
MEASUREMENT OF BLOOD CONSTITUENTS**

**RELATED APPLICATIONS**

**[0001]** This application claims the benefit of priority under 35 U.S.C. § 119(e) of the following U.S. Provisional Patent Applications:

<u>App. No.</u>	<u>Filing Date</u>	<u>Title</u>	<u>Attorney Docket</u>
61/086,060	8/4/08	<i>Multi-Stream Data Collection System For Non-Invasive Measurement of Glucose and Other Analytes</i>	MLHUM.002PR
61/086,108	8/4/08	<i>Multi-Stream Sensor Front Ends for Noninvasive Measurement of Glucose and Other Analytes</i>	MLHUM.003PR
61/086,063	8/4/08	<i>Multi-Stream Detector For Noninvasive Measurement Of Glucose And Other Analytes</i>	MLHUM.004PR
61/086,057	8/4/08	<i>Multi-Stream Emitter For Noninvasive Measurement Of Glucose And Other Analytes</i>	MLHUM.005PR
61/091,732	8/25/08	<i>Sensor For Improving Measurement Of Blood Constituents</i>	MLHUM.011PR

**[0002]** This application is related to the following U.S. Patent Applications:

<u>App. No.</u>	<u>Filing Date</u>	<u>Title</u>	<u>Attorney Docket</u>
12/497,528	7/2/09	<i>Noise Shielding for Noninvasive Device Contoured Protrusion for Improving Spectroscopic Measurement of Blood Constituents</i>	MLHUM.006A
12/497,523	7/2/09	<i>Heat Sink for Noninvasive Medical Sensor</i>	MLHUM.011A
Unknown	Herewith	<i>Multi-Stream Sensor Front Ends for Non-Invasive Measurement of Blood Constituents</i>	MLHUM.003A
Unknown	Herewith	<i>Multi-Stream Sensor for Non-Invasive Measurement of Blood Constituents</i>	MLHUM.004A
Unknown	Herewith	<i>Multi-Stream Emitter for Non-Invasive Measurement of Blood Constituents</i>	MLHUM.005A

**[0003]** The foregoing applications are hereby incorporated by reference in their entirety.

#### BACKGROUND

**[0004]** The standard of care in caregiver environments includes patient monitoring through spectroscopic analysis using, for example, a pulse oximeter. Devices capable of spectroscopic analysis generally include a light source(s) transmitting optical radiation into or reflecting off a measurement site, such as, body tissue carrying pulsing blood. After attenuation by tissue and fluids of the measurement site, a photodetection device(s) detects the attenuated light and outputs a detector signal(s) responsive to the detected attenuated light. A signal processing device(s) process the detector(s) signal(s) and outputs a measurement indicative of a blood constituent of interest, such as glucose, oxygen, met hemoglobin, total hemoglobin, other physiological parameters, or other data or combinations of data useful in determining a state or trend of wellness of a patient.

**[0005]** In noninvasive devices and methods, a sensor is often adapted to position a finger proximate the light source and light detector. For example, noninvasive sensors often include a clothespin-shaped housing that includes a contoured bed conforming generally to the shape of a finger.

## SUMMARY

**[0006]** This disclosure describes embodiments of noninvasive methods, devices, and systems for measuring a blood constituent or analyte, such as oxygen, carbon monoxide, methemoglobin, total hemoglobin, glucose, proteins, glucose, lipids, a percentage thereof (e.g., saturation) or for measuring many other physiologically relevant patient characteristics. These characteristics can relate, for example, to pulse rate, hydration, trending information and analysis, and the like.

**[0007]** In an embodiment, the system includes a noninvasive sensor and a patient monitor communicating with the noninvasive sensor. The non-invasive sensor may include different architectures to implement some or all of the disclosed features. In addition, an artisan will recognize that the non-invasive sensor may include or may be coupled to other components, such as a network interface, and the like. Moreover, the patient monitor may include a display device, a network interface communicating with any one or combination of a computer network, a handheld computing device, a mobile phone, the Internet, or the like. In addition, embodiments may include multiple optical sources that emit light at a plurality of wavelengths and that are arranged from the perspective of the light detector(s) as a point source.

**[0008]** In an embodiment, a noninvasive device is capable of producing a signal responsive to light attenuated by tissue at a measurement site. The device may comprise an optical source and a plurality of photodetectors. The optical source is configured to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm. The photodetectors are configured to detect the optical radiation from said optical source after attenuation by the tissue of the measurement site and each output a respective signal stream responsive to the detected optical radiation.

**[0009]** In an embodiment, a noninvasive, physiological sensor is capable of outputting a signal responsive to a blood analyte present in a monitored patient. The sensor may comprise a sensor housing, an optical source, and photodetectors. The optical source is positioned by the housing with respect to a tissue site of a patient when said housing is applied to the patient. The photodetectors are

positioned by the housing with respect to said tissue site when the housing is applied to the patient with a variation in path length among at least some of the photodetectors from the optical source. The photodetectors are configured to detect a sequence of optical radiation from the optical source after attenuation by tissue of the tissue site. The photodetectors may be each configured to output a respective signal stream responsive to the detected sequence of optical radiation. An output signal responsive to one or more of the signal streams is then usable to determine the blood analyte based at least in part on the variation in path length

**[0010]** In an embodiment, a method of measuring an analyte based on multiple streams of optical radiation measured from a measurement site is provided. A sequence of optical radiation pulses is emitted to the measurement site. At a first location, a first stream of optical radiation is detected from the measurement site. At least at one additional location different from the first location, an additional stream of optical radiation is detected from the measurement site. An output measurement value indicative of the analyte is then determined based on the detected streams of optical radiation.

**[0011]** For purposes of summarizing the disclosure, certain aspects, advantages and novel features of the inventions have been described herein. It is to be understood that not necessarily all such advantages can be achieved in accordance with any particular embodiment of the inventions disclosed herein. Thus, the inventions disclosed herein can be embodied or carried out in a manner that achieves or optimizes one advantage or group of advantages as taught herein without necessarily achieving other advantages as can be taught or suggested herein.



### BRIEF DESCRIPTION OF THE DRAWINGS

**[0012]** Throughout the drawings, reference numbers can be re-used to indicate correspondence between referenced elements. The drawings are provided to illustrate embodiments of the inventions described herein and not to limit the scope thereof.

**[0013]** FIGURE 1 illustrates a block diagram of an example data collection system capable of noninvasively measuring one or more blood analytes in a monitored patient, according to an embodiment of the disclosure;

**[0014]** FIGURES 2A – 2D illustrate an exemplary handheld monitor and an exemplary noninvasive optical sensor of the patient monitoring system of Figure 1, according to embodiments of the disclosure;

**[0015]** FIGURES 3A – 3C illustrate side and perspective views of an exemplary noninvasive sensor housing including a finger bed protrusion and heat sink, according to an embodiment of the disclosure;

**[0016]** FIGURE 3D illustrates a side view of another example noninvasive sensor housing including a heat sink, according to an embodiment of the disclosure;

**[0017]** FIGURE 3E illustrates a perspective view of an example noninvasive sensor detector shell including example detectors, according to an embodiment of the disclosure;

**[0018]** FIGURE 3F illustrates a side view of an example noninvasive sensor housing including a finger bed protrusion and heat sink, according to an embodiment of the disclosure;

**[0019]** FIGURES 4A through 4C illustrate top elevation, side and top perspective views of an example protrusion, according to an embodiment of the disclosure;

**[0020]** FIGURE 5 illustrates an example graph depicting possible effects of a protrusion on light transmittance, according to an embodiment of the disclosure;

**[0021]** FIGURES 6A through 6D illustrate perspective, front elevation, side and top views of another example protrusion, according to an embodiment of the disclosure;

**[0022]** FIGURE 6E illustrates an example sensor incorporating the protrusion of FIGURES 6A through 6D, according to an embodiment of the disclosure;

**[0023]** FIGURES 7A through 7B illustrate example arrangements of conductive glass that may be employed in the system of FIGURE 1, according to embodiments of the disclosure.

**[0024]** FIGURES 8A through 8D illustrate an example top elevation view, side views, and a bottom elevation view of the conductive glass that may be employed in the system of FIGURE 1, according to embodiments of the disclosure;

**[0025]** FIGURE 9 shows example comparative results obtained by an embodiment of a sensor;

**[0026]** FIGURES 10A and 10B illustrate comparative noise floors of various embodiments of the present disclosure;

**[0027]** FIGURE 11A illustrates an exemplary emitter that may be employed in the sensor, according to an embodiment of the disclosure;

**[0028]** FIGURE 11B illustrates a configuration of emitting optical radiation into a measurement site for measuring blood constituents, according to an embodiment of the disclosure;

**[0029]** FIGURE 11C illustrates another exemplary emitter that may be employed in the sensor according to an embodiment of the disclosure;

**[0030]** FIGURE 11D illustrates another exemplary emitter that may be employed in the sensor according to an embodiment of the disclosure.

**[0031]** FIGURE 12A illustrates an example detector portion that may be employed in an embodiment of a sensor, according to an embodiment of the disclosure;

**[0032]** FIGURES 12B through 12D illustrate exemplary arrangements of detectors that may be employed in an embodiment of the sensor, according to some embodiments of the disclosure;

**[0033]** FIGURES 12E through 12H illustrate exemplary structures of photodiodes that may be employed in embodiments of the detectors, according to some embodiments of the disclosure;

**[0034]** FIGURE 13 illustrates an example multi-stream operation of the system of FIGURE 1, according to an embodiment of the disclosure;

**[0035]** FIGURE 14A illustrates another example detector portion having a partially cylindrical protrusion that can be employed in an embodiment of a sensor, according to an embodiment of the disclosure;

**[0036]** FIGURE 14B depicts a front elevation view of the partially cylindrical protrusion of FIGURE 14A;

**[0037]** FIGURES 14C through 14E illustrate embodiments of a detector submount;

**[0038]** FIGURES 14F through 14H illustrate embodiment of portions of a detector shell;

**[0039]** FIGURE 14I illustrates a cutaway view of an embodiment of a sensor;

**[0040]** FIGURES 15A through 15F illustrate embodiments of sensors that include heat sink features;

**[0041]** FIGURES 15G and 15H illustrate embodiments of connector features that can be used with any of the sensors described herein;

**[0042]** FIGURE 15I illustrates an exemplary architecture for a transimpedance-based front-end that may be employed in any of the sensors described herein;

**[0043]** FIGURE 15J illustrates an exemplary noise model for configuring the transimpedance-based front-ends shown in FIGURE 15I;

**[0044]** FIGURE 15K shows different architectures and layouts for various embodiments of a sensor and its detectors;

**[0045]** FIGURE 15L illustrates an exemplary architecture for a switched-capacitor-based front-end that may be employed in any of the sensors described herein;

**[0046]** FIGURES 16A and 16B illustrate embodiments of disposable optical sensors;

**[0047]** FIGURE 17 illustrates an exploded view of certain components of an example sensor; and

**[0048]** FIGURES 18 through 22 illustrate various results obtained by an exemplary sensor of the disclosure.

#### DETAILED DESCRIPTION

**[0049]** The present disclosure generally relates to non-invasive medical devices. In the present disclosure, a sensor can measure various blood constituents or analytes noninvasively using multi-stream spectroscopy. In an embodiment, the multi-stream spectroscopy can employ visible, infrared and near infrared wavelengths. As disclosed herein, the sensor is capable of noninvasively measuring blood analytes or percentages thereof (e.g., saturation) based on various combinations of features and components.

**[0050]** The sensor can include photocommunicative components, such as an emitter, a detector, and other components. The emitter can include a plurality of sets of optical sources that, in an embodiment, are arranged together as a point source. The various optical sources can emit a sequence of optical radiation pulses at different wavelengths towards a measurement site, such as a patient's finger. Detectors can then detect optical radiation from the measurement site. The optical sources and optical radiation detectors can operate at any appropriate wavelength, including, as discussed herein, infrared, near infrared, visible light, and ultraviolet. In addition, the optical sources and optical radiation detectors can operate at any appropriate wavelength, and such modifications to the embodiments desirable to operate at any such wavelength will be apparent to those skilled in the art.

**[0051]** In certain embodiments, multiple detectors are employed and arranged in a spatial geometry. This spatial geometry provides a diversity of path lengths among at least some of the detectors and allows for multiple bulk and pulsatile measurements that are robust. Each of the detectors can provide a respective output stream based on the detected optical radiation, or a sum of output streams can be provided from multiple detectors. In some embodiments, the sensor can also include other components, such as one or more heat sinks and one or more thermistors.

**[0052]** The sensor can be coupled to one or more monitors that process and/or display the sensor's output. The monitors can include various components, such as a sensor front end, a signal processor, a display, etc.

**[0053]** The sensor can be integrated with a monitor, for example, into a handheld unit including the sensor, a display and user controls. In other embodiments, the sensor can communicate with one or more processing devices. The communication can be via wire(s), cable(s), flex circuit(s), wireless technologies, or other suitable analog or digital communication methodologies and devices to perform those methodologies. Many of the foregoing arrangements allow the sensor to be attached to the measurement site while the device is attached elsewhere on a patient, such as the patient's arm, or placed at a location near the patient, such as a bed, shelf or table. The sensor or monitor can also provide outputs to a storage device or network interface.

**[0054]** Reference will now be made to the Figures to discuss embodiments of the present disclosure.

**[0055]** **FIGURE 1** illustrates an example of a data collection system 100. In certain embodiments, the data collection system 100 noninvasively measure a blood analyte, such as oxygen, carbon monoxide, methemoglobin, total hemoglobin, glucose, proteins, lipids, a percentage thereof (e.g., saturation) or for measuring many other physiologically relevant patient characteristics. The system 100 can also measure additional blood analytes and/or other physiological parameters useful in determining a state or trend of wellness of a patient.

**[0056]** The data collection system 100 can be capable of measuring optical radiation from the measurement site. For example, in some embodiments, the data collection system 100 can employ photodiodes defined in terms of area. In an embodiment, the area is from about  $1 \text{ mm}^2$  –  $5 \text{ mm}^2$  (or higher) that are capable of detecting about 100 nanoamps (nA) or less of current resulting from measured light at full scale. In addition to having its ordinary meaning, the phrase “at full scale” can mean light saturation of a photodiode amplifier (not shown). Of course, as would be understood by a person of skill in the art from the present disclosure, various other sizes and types of photodiodes can be used with the embodiments of the present disclosure.

**[0057]** The data collection system 100 can measure a range of approximately about 2 nA to about 100 nA full scale. The data collection system

100 can also include sensor front-ends that are capable of processing and amplifying current from the detector(s) at signal-to-noise ratios (SNRs) of about 100 decibels (dB) or more, such as about 120 dB in order to measure various desired analytes. The data collection system 100 can operate with a lower SNR if less accuracy is desired for an analyte like glucose.

**[0058]** The data collection system 100 can measure analyte concentrations, including glucose, at least in part by detecting light attenuated by a measurement site 102. The measurement site 102 can be any location on a patient's body, such as a finger, foot, ear lobe, or the like. For convenience, this disclosure is described primarily in the context of a finger measurement site 102. However, the features of the embodiments disclosed herein can be used with other measurement sites 102.

**[0059]** In the depicted embodiment, the system 100 includes an optional tissue thickness adjuster or tissue shaper 105, which can include one or more protrusions, bumps, lenses, or other suitable tissue-shaping mechanisms. In certain embodiments, the tissue shaper 105 is a flat or substantially flat surface that can be positioned proximate the measurement site 102 and that can apply sufficient pressure to cause the tissue of the measurement site 102 to be flat or substantially flat. In other embodiments, the tissue shaper 105 is a convex or substantially convex surface with respect to the measurement site 102. Many other configurations of the tissue shaper 105 are possible. Advantageously, in certain embodiments, the tissue shaper 105 reduces thickness of the measurement site 102 while preventing or reducing occlusion at the measurement site 102. Reducing thickness of the site can advantageously reduce the amount of attenuation of the light because there is less tissue through which the light must travel. Shaping the tissue in to a convex (or alternatively concave) surface can also provide more surface area from which light can be detected.

**[0060]** The embodiment of the data collection system 100 shown also includes an optional noise shield 103. In an embodiment, the noise shield 103 can be advantageously adapted to reduce electromagnetic noise while increasing the transmittance of light from the measurement site 102 to one or more detectors 106

(described below). For example, the noise shield 103 can advantageously include a conductive coated glass or metal grid electrically communicating with one or more other shields of the sensor 101 or electrically grounded. In an embodiment where the noise shield 103 includes conductive coated glass, the coating can advantageously include indium tin oxide. In an embodiment, the indium tin oxide includes a surface resistivity ranging from approximately 30 ohms per square inch to about 500 ohms per square inch. In an embodiment, the resistivity is approximately 30, 200, or 500 ohms per square inch. As would be understood by a person of skill in the art from the present disclosure, other resistivities can also be used which are less than about 30 ohms or more than about 500 ohms. Other conductive materials transparent or substantially transparent to light can be used instead.

**[0061]** In some embodiments, the measurement site 102 is located somewhere along a non-dominant arm or a non-dominant hand, e.g., a right-handed person's left arm or left hand. In some patients, the non-dominant arm or hand can have less musculature and higher fat content, which can result in less water content in that tissue of the patient. Tissue having less water content can provide less interference with the particular wavelengths that are absorbed in a useful manner by blood analytes like glucose. Accordingly, in some embodiments, the data collection system 100 can be used on a person's non-dominant hand or arm.

**[0062]** The data collection system 100 can include a sensor 101 (or multiple sensors) that is coupled to a processing device or physiological monitor 109. In an embodiment, the sensor 101 and the monitor 109 are integrated together into a single unit. In another embodiment, the sensor 101 and the monitor 109 are separate from each other and communicate one with another in any suitable manner, such as via a wired or wireless connection. The sensor 101 and monitor 109 can be attachable and detachable from each other for the convenience of the user or caregiver, for ease of storage, sterility issues, or the like. The sensor 101 and the monitor 109 will now be further described.

**[0063]** In the depicted embodiment shown in **FIGURE 1**, the sensor 101 includes an emitter 104, a tissue shaper 105, a set of detectors 106, and a front-end interface 108. The emitter 104 can serve as the source of optical radiation



transmitted towards measurement site 102. As will be described in further detail below, the emitter 104 can include one or more sources of optical radiation, such as LEDs, laser diodes, incandescent bulbs with appropriate frequency-selective filters, combinations of the same, or the like. In an embodiment, the emitter 104 includes sets of optical sources that are capable of emitting visible and near-infrared optical radiation.

**[0064]** In some embodiments, the emitter 104 is used as a point optical source, and thus, the one or more optical sources of the emitter 104 can be located within a close distance to each other, such as within about a 2 mm to about 4 mm. The emitters 104 can be arranged in an array, such as is described in U.S. Publication No. 2006/0211924, filed Sept. 21, 2006, titled "Multiple Wavelength Sensor Emitters," the disclosure of which is hereby incorporated by reference in its entirety. In particular, the emitters 104 can be arranged at least in part as described in paragraphs [0061] through [0068] of the aforementioned publication, which paragraphs are hereby incorporated specifically by reference. Other relative spatial relationships can be used to arrange the emitters 104.

**[0065]** For analytes like glucose, currently available non-invasive techniques often attempt to employ light near the water absorbance minima at or about 1600 nm. Typically, these devices and methods employ a single wavelength or single band of wavelengths at or about 1600 nm. However, to date, these techniques have been unable to adequately consistently measure analytes like glucose based on spectroscopy.

**[0066]** In contrast, the emitter 104 of the data collection system 100 can emit, in certain embodiments, combinations of optical radiation in various bands of interest. For example, in some embodiments, for analytes like glucose, the emitter 104 can emit optical radiation at three (3) or more wavelengths between about 1600 nm to about 1700 nm. In particular, the emitter 104 can emit optical radiation at or about 1610 nm, about 1640 nm, and about 1665 nm. In some circumstances, the use of three wavelengths within about 1600 nm to about 1700 nm enable sufficient SNRs of about 100 dB, which can result in a measurement accuracy of about 20 mg/dL or better for analytes like glucose.

**[0067]** In other embodiments, the emitter 104 can use two (2) wavelengths within about 1600 nm to about 1700 nm to advantageously enable SNRs of about 85 dB, which can result in a measurement accuracy of about 25-30 mg/dL or better for analytes like glucose. Furthermore, in some embodiments, the emitter 104 can emit light at wavelengths above about 1670 nm. Measurements at these wavelengths can be advantageously used to compensate or confirm the contribution of protein, water, and other non-hemoglobin species exhibited in measurements for analytes like glucose conducted between about 1600 nm and about 1700 nm. Of course, other wavelengths and combinations of wavelengths can be used to measure analytes and/or to distinguish other types of tissue, fluids, tissue properties, fluid properties, combinations of the same or the like.

**[0068]** For example, the emitter 104 can emit optical radiation across other spectra for other analytes. In particular, the emitter 104 can employ light wavelengths to measure various blood analytes or percentages (e.g., saturation) thereof. For example, in one embodiment, the emitter 104 can emit optical radiation in the form of pulses at wavelengths about 905 nm, about 1050 nm, about 1200 nm, about 1300 nm, about 1330 nm, about 1610 nm, about 1640 nm, and about 1665 nm. In another embodiment, the emitter 104 can emit optical radiation ranging from about 860 nm to about 950 nm, about 950 nm to about 1100 nm, about 1100 nm to about 1270 nm, about 1250 nm to about 1350 nm, about 1300 nm to about 1360 nm, and about 1590 nm to about 1700 nm. Of course, the emitter 104 can transmit any of a variety of wavelengths of visible or near-infrared optical radiation.

**[0069]** Due to the different responses of analytes to the different wavelengths, certain embodiments of the data collection system 100 can advantageously use the measurements at these different wavelengths to improve the accuracy of measurements. For example, the measurements of water from visible and infrared light can be used to compensate for water absorbance that is exhibited in the near-infrared wavelengths.

**[0070]** As briefly described above, the emitter 104 can include sets of light-emitting diodes (LEDs) as its optical source. The emitter 104 can use one or

more top-emitting LEDs. In particular, in some embodiments, the emitter 104 can include top-emitting LEDs emitting light at about 850 nm to 1350 nm.

**[0071]** The emitter 104 can also use super luminescent LEDs (SLEDs) or side-emitting LEDs. In some embodiments, the emitter 104 can employ SLEDs or side-emitting LEDs to emit optical radiation at about 1600 nm to about 1800 nm. Emitter 104 can use SLEDs or side-emitting LEDs to transmit near infrared optical radiation because these types of sources can transmit at high power or relatively high power, e.g., about 40 mW to about 100 mW. This higher power capability can be useful to compensate or overcome the greater attenuation of these wavelengths of light in tissue and water. For example, the higher power emission can effectively compensate and/or normalize the absorption signal for light in the mentioned wavelengths to be similar in amplitude and/or effect as other wavelengths that can be detected by one or more photodetectors after absorption. However, the embodiments of the present disclosure do not necessarily require the use of high power optical sources. For example, some embodiments may be configured to measure analytes, such as total hemoglobin (tHb), oxygen saturation (SpO<sub>2</sub>), carboxyhemoglobin, methemoglobin, etc., without the use of high power optical sources like side emitting LEDs. Instead, such embodiments may employ other types of optical sources, such as top emitting LEDs. Alternatively, the emitter 104 can use other types of sources of optical radiation, such as a laser diode, to emit near-infrared light into the measurement site 102.

**[0072]** In addition, in some embodiments, in order to assist in achieving a comparative balance of desired power output between the LEDs, some of the LEDs in the emitter 104 can have a filter or covering that reduces and/or cleans the optical radiation from particular LEDs or groups of LEDs. For example, since some wavelengths of light can penetrate through tissue relatively well, LEDs, such as some or all of the top-emitting LEDs can use a filter or covering, such as a cap or painted dye. This can be useful in allowing the emitter 104 to use LEDs with a higher output and/or to equalize intensity of LEDs.

**[0073]** The data collection system 100 also includes a driver 111 that drives the emitter 104. The driver 111 can be a circuit or the like that is controlled

by the monitor 109. For example, the driver 111 can provide pulses of current to the emitter 104. In an embodiment, the driver 111 drives the emitter 104 in a progressive fashion, such as in an alternating manner. The driver 111 can drive the emitter 104 with a series of pulses of about 1 milliwatt (mW) for some wavelengths that can penetrate tissue relatively well and from about 40 mW to about 100 mW for other wavelengths that tend to be significantly absorbed in tissue. A wide variety of other driving powers and driving methodologies can be used in various embodiments.

**[0074]** The driver 111 can be synchronized with other parts of the sensor 101 and can minimize or reduce jitter in the timing of pulses of optical radiation emitted from the emitter 104. In some embodiments, the driver 111 is capable of driving the emitter 104 to emit optical radiation in a pattern that varies by less than about 10 parts-per-million.

**[0075]** The detectors 106 capture and measure light from the measurement site 102. For example, the detectors 106 can capture and measure light transmitted from the emitter 104 that has been attenuated or reflected from the tissue in the measurement site 102. The detectors 106 can output a detector signal 107 responsive to the light captured or measured. The detectors 106 can be implemented using one or more photodiodes, phototransistors, or the like.

**[0076]** In addition, the detectors 106 can be arranged with a spatial configuration to provide a variation of path lengths among at least some of the detectors 106. That is, some of the detectors 106 can have the substantially, or from the perspective of the processing algorithm, effectively, the same path length from the emitter 104. However, according to an embodiment, at least some of the detectors 106 can have a different path length from the emitter 104 relative to other of the detectors 106. Variations in path lengths can be helpful in allowing the use of a bulk signal stream from the detectors 106. In some embodiments, the detectors 106 may employ a linear spacing, a logarithmic spacing, or a two or three dimensional matrix of spacing, or any other spacing scheme in order to provide an appropriate variation in path lengths.

**[0077]** The front end interface 108 provides an interface that adapts the output of the detectors 106, which is responsive to desired physiological parameters. For example, the front end interface 108 can adapt a signal 107 received from one or more of the detectors 106 into a form that can be processed by the monitor 109, for example, by a signal processor 110 in the monitor 109. The front end interface 108 can have its components assembled in the sensor 101, in the monitor 109, in connecting cabling (if used), combinations of the same, or the like. The location of the front end interface 108 can be chosen based on various factors including space desired for components, desired noise reductions or limits, desired heat reductions or limits, and the like.

**[0078]** The front end interface 108 can be coupled to the detectors 106 and to the signal processor 110 using a bus, wire, electrical or optical cable, flex circuit, or some other form of signal connection. The front end interface 108 can also be at least partially integrated with various components, such as the detectors 106. For example, the front end interface 108 can include one or more integrated circuits that are on the same circuit board as the detectors 106. Other configurations can also be used.

**[0079]** The front end interface 108 can be implemented using one or more amplifiers, such as transimpedance amplifiers, that are coupled to one or more analog to digital converters (ADCs) (which can be in the monitor 109), such as a sigma-delta ADC. A transimpedance-based front end interface 108 can employ single-ended circuitry, differential circuitry, and/or a hybrid configuration. A transimpedance-based front end interface 108 can be useful for its sampling rate capability and freedom in modulation/demodulation algorithms. For example, this type of front end interface 108 can advantageously facilitate the sampling of the ADCs being synchronized with the pulses emitted from the emitter 104.

**[0080]** The ADC or ADCs can provide one or more outputs into multiple channels of digital information for processing by the signal processor 110 of the monitor 109. Each channel can correspond to a signal output from a detector 106.

**[0081]** In some embodiments, a programmable gain amplifier (PGA) can be used in combination with a transimpedance-based front end interface 108. For

example, the output of a transimpedance-based front end interface 108 can be output to a PGA that is coupled with an ADC in the monitor 109. A PGA can be useful in order to provide another level of amplification and control of the stream of signals from the detectors 106. Alternatively, the PGA and ADC components can be integrated with the transimpedance-based front end interface 108 in the sensor 101.

**[0082]** In another embodiment, the front end interface 108 can be implemented using switched-capacitor circuits. A switched-capacitor-based front end interface 108 can be useful for, in certain embodiments, its resistor-free design and analog averaging properties. In addition, a switched-capacitor-based front end interface 108 can be useful because it can provide a digital signal to the signal processor 110 in the monitor 109.

**[0083]** As shown in **FIGURE 1**, the monitor 109 can include the signal processor 110 and a user interface, such as a display 112. The monitor 109 can also include optional outputs alone or in combination with the display 112, such as a storage device 114 and a network interface 116. In an embodiment, the signal processor 110 includes processing logic that determines measurements for desired analytes, such as glucose, based on the signals received from the detectors 106. The signal processor 110 can be implemented using one or more microprocessors or subprocessors (e.g., cores), digital signal processors, application specific integrated circuits (ASICs), field programmable gate arrays (FPGAs), combinations of the same, and the like.

**[0084]** The signal processor 110 can provide various signals that control the operation of the sensor 101. For example, the signal processor 110 can provide an emitter control signal to the driver 111. This control signal can be useful in order to synchronize, minimize, or reduce jitter in the timing of pulses emitted from the emitter 104. Accordingly, this control signal can be useful in order to cause optical radiation pulses emitted from the emitter 104 to follow a precise timing and consistent pattern. For example, when a transimpedance-based front end interface 108 is used, the control signal from the signal processor 110 can provide synchronization with the ADC in order to avoid aliasing, cross-talk, and the like. As

also shown, an optional memory 113 can be included in the front-end interface 108 and/or in the signal processor 110. This memory 113 can serve as a buffer or storage location for the front-end interface 108 and/or the signal processor 110, among other uses.

**[0085]** The user interface 112 can provide an output, e.g., on a display, for presentation to a user of the data collection system 100. The user interface 112 can be implemented as a touch-screen display, an LCD display, an organic LED display, or the like. In addition, the user interface 112 can be manipulated to allow for measurement on the non-dominant side of patient. For example, the user interface 112 can include a flip screen, a screen that can be moved from one side to another on the monitor 109, or can include an ability to reorient its display indicia responsive to user input or device orientation. In alternative embodiments, the data collection system 100 can be provided without a user interface 112 and can simply provide an output signal to a separate display or system.

**[0086]** A storage device 114 and a network interface 116 represent other optional output connections that can be included in the monitor 109. The storage device 114 can include any computer-readable medium, such as a memory device, hard disk storage, EEPROM, flash drive, or the like. The various software and/or firmware applications can be stored in the storage device 114, which can be executed by the signal processor 110 or another processor of the monitor 109. The network interface 116 can be a serial bus port (RS-232/RS-485), a Universal Serial Bus (USB) port, an Ethernet port, a wireless interface (e.g., WiFi such as any 802.1x interface, including an internal wireless card), or other suitable communication device(s) that allows the monitor 109 to communicate and share data with other devices. The monitor 109 can also include various other components not shown, such as a microprocessor, graphics processor, or controller to output the user interface 112, to control data communications, to compute data trending, or to perform other operations.

**[0087]** Although not shown in the depicted embodiment, the data collection system 100 can include various other components or can be configured in different ways. For example, the sensor 101 can have both the emitter 104 and

detectors 106 on the same side of the measurement site 102 and use reflectance to measure analytes. The data collection system 100 can also include a sensor that measures the power of light emitted from the emitter 104.

**[0088]** FIGURES 2A through 2D illustrate example monitoring devices 200 in which the data collection system 100 can be housed. Advantageously, in certain embodiments, some or all of the example monitoring devices 200 shown can have a shape and size that allows a user to operate it with a single hand or attach it, for example, to a patient's body or limb. Although several examples are shown, many other monitoring device configurations can be used to house the data collection system 100. In addition, certain of the features of the monitoring devices 200 shown in FIGURES 2A through 2D can be combined with features of the other monitoring devices 200 shown.

**[0089]** Referring specifically to **FIGURE 2A**, an example monitoring device 200A is shown, in which a sensor 201a and a monitor 209a are integrated into a single unit. The monitoring device 200A shown is a handheld or portable device that can measure glucose and other analytes in a patient's finger. The sensor 201a includes an emitter shell 204a and a detector shell 206a. The depicted embodiment of the monitoring device 200A also includes various control buttons 208a and a display 210a.

**[0090]** The sensor 201a can be constructed of white material used for reflective purposes (such as white silicone or plastic), which can increase the usable signal at the detector 106 by forcing light back into the sensor 201a. Pads in the emitter shell 204a and the detector shell 206a can contain separated windows to prevent or reduce mixing of light signals, for example, from distinct quadrants on a patient's finger. In addition, these pads can be made of a relatively soft material, such as a gel or foam, in order to conform to the shape, for example, of a patient's finger. The emitter shell 204a and the detector shell 206a can also include absorbing black or grey material portions to prevent or reduce ambient light from entering into the sensor 201a.

**[0091]** In some embodiments, some or all portions of the emitter shell 204a and/or detector shell 206a can be detachable and/or disposable. For



example, some or all portions of the shells 204a and 206a can be removable pieces. The removability of the shells 204a and 206a can be useful for sanitary purposes or for sizing the sensor 201a to different patients. The monitor 209a can include a fitting, slot, magnet, or other connecting mechanism to allow the sensor 201c to be removably attached to the monitor 209a.

**[0092]** The monitoring device 200a also includes optional control buttons 208a and a display 210a that can allow the user to control the operation of the device. For example, a user can operate the control buttons 208a to view one or more measurements of various analytes, such as glucose. In addition, the user can operate the control buttons 208a to view other forms of information, such as graphs, histograms, measurement data, trend measurement data, parameter combination views, wellness indications, and the like. Many parameters, trends, alarms and parameter displays could be output to the display 210a, such as those that are commercially available through a wide variety of noninvasive monitoring devices from Masimo<sup>®</sup> Corporation of Irvine, California.

**[0093]** Furthermore, the controls 208a and/or display 210a can provide functionality for the user to manipulate settings of the monitoring device 200a, such as alarm settings, emitter settings, detector settings, and the like. The monitoring device 200a can employ any of a variety of user interface designs, such as frames, menus, touch-screens, and any type of button.

**[0094]** **FIGURE 2B** illustrates another example of a monitoring device 200B. In the depicted embodiment, the monitoring device 200B includes a finger clip sensor 201b connected to a monitor 209b via a cable 212. In the embodiment shown, the monitor 209b includes a display 210b, control buttons 208b and a power button. Moreover, the monitor 209b can advantageously include electronic processing, signal processing, and data storage devices capable of receiving signal data from said sensor 201b, processing the signal data to determine one or more output measurement values indicative of one or more physiological parameters of a monitored patient, and displaying the measurement values, trends of the measurement values, combinations of measurement values, and the like.

**[0095]** The cable 212 connecting the sensor 201b and the monitor 209b can be implemented using one or more wires, optical fiber, flex circuits, or the like. In some embodiments, the cable 212 can employ twisted pairs of conductors in order to minimize or reduce cross-talk of data transmitted from the sensor 201b to the monitor 209b. Various lengths of the cable 212 can be employed to allow for separation between the sensor 201b and the monitor 209b. The cable 212 can be fitted with a connector (male or female) on either end of the cable 212 so that the sensor 201b and the monitor 209b can be connected and disconnected from each other. Alternatively, the sensor 201b and the monitor 209b can be coupled together via a wireless communication link, such as an infrared link, radio frequency channel, or any other wireless communication protocol and channel.

**[0096]** The monitor 209b can be attached to the patient. For example, the monitor 209b can include a belt clip or straps (see, e.g., FIGURE 2C) that facilitate attachment to a patient's belt, arm, leg, or the like. The monitor 209b can also include a fitting, slot, magnet, LEMO snap-click connector, or other connecting mechanism to allow the cable 212 and sensor 201b to be attached to the monitor 209B.

**[0097]** The monitor 209b can also include other components, such as a speaker, power button, removable storage or memory (e.g., a flash card slot), an AC power port, and one or more network interfaces, such as a universal serial bus interface or an Ethernet port. For example, the monitor 209b can include a display 210b that can indicate a measurement for glucose, for example, in mg/dL. Other analytes and forms of display can also appear on the monitor 209b.

**[0098]** In addition, although a single sensor 201b with a single monitor 209b is shown, different combinations of sensors and device pairings can be implemented. For example, multiple sensors can be provided for a plurality of differing patient types or measurement sites or even patient fingers.

**[0099]** **FIGURE 2C** illustrates yet another example of monitoring device 200C that can house the data collection system 100. Like the monitoring device 200B, the monitoring device 200C includes a finger clip sensor 201c connected to a monitor 209c via a cable 212. The cable 212 can have all of the features described

above with respect to FIGURE 2B. The monitor 209c can include all of the features of the monitor 200B described above. For example, the monitor 209c includes buttons 208c and a display 210c. The monitor 209c shown also includes straps 214c that allow the monitor 209c to be attached to a patient's limb or the like.

**[0100] FIGURE 2D** illustrates yet another example of monitoring device 200D that can house the data collection system 100. Like the monitoring devices 200B and 200C, the monitoring device 200D includes a finger clip sensor 201d connected to a monitor 209d via a cable 212. The cable 212 can have all of the features described above with respect to FIGURE 2B. In addition to having some or all of the features described above with respect to FIGURES 2B and 2C, the monitoring device 200D includes an optional universal serial bus (USB) port 216 and an Ethernet port 218. The USB port 216 and the Ethernet port 218 can be used, for example, to transfer information between the monitor 209d and a computer (not shown) via a cable. Software stored on the computer can provide functionality for a user to, for example, view physiological data and trends, adjust settings and download firmware updates to the monitor 209b, and perform a variety of other functions. The USB port 216 and the Ethernet port 218 can be included with the other monitoring devices 200A, 200B, and 200C described above.

**[0101] FIGURES 3A through 3C** illustrate more detailed examples of embodiments of a sensor 301a. The sensor 301a shown can include all of the features of the sensors 100 and 200 described above.

**[0102]** Referring to **FIGURE 3A**, the sensor 301a in the depicted embodiment is a clothespin-shaped clip sensor that includes an enclosure 302a for receiving a patient's finger. The enclosure 302a is formed by an upper section or emitter shell 304a, which is pivotably connected with a lower section or detector shell 306a. The emitter shell 304a can be biased with the detector shell 306a to close together around a pivot point 303a and thereby sandwich finger tissue between the emitter and detector shells 304a, 306a.

**[0103]** In an embodiment, the pivot point 303a advantageously includes a pivot capable of adjusting the relationship between the emitter and detector shells 304a, 306a to effectively level the sections when applied to a tissue site. In another

embodiment, the sensor 301a includes some or all features of the finger clip described in U.S. Publication No. 2006/0211924, incorporated above, such as a spring that causes finger clip forces to be distributed along the finger. Paragraphs [0096] through [0105], which describe this feature, are hereby specifically incorporated by reference.

**[0104]** The emitter shell 304a can position and house various emitter components of the sensor 301a. It can be constructed of reflective material (e.g., white silicone or plastic) and/or can be metallic or include metalized plastic (e.g., including carbon and aluminum) to possibly serve as a heat sink. The emitter shell 304a can also include absorbing opaque material, such as, for example, black or grey colored material, at various areas, such as on one or more flaps 307a, to reduce ambient light entering the sensor 301a.

**[0105]** The detector shell 306a can position and house one or more detector portions of the sensor 301a. The detector shell 306a can be constructed of reflective material, such as white silicone or plastic. As noted, such materials can increase the usable signal at a detector by forcing light back into the tissue and measurement site (see FIGURE 1). The detector shell 306a can also include absorbing opaque material at various areas, such as lower area 308a, to reduce ambient light entering the sensor 301a.

**[0106]** Referring to **FIGURES 3B** and **3C**, an example of finger bed 310 is shown in the sensor 301b. The finger bed 310 includes a generally curved surface shaped generally to receive tissue, such as a human digit. The finger bed 310 includes one or more ridges or channels 314. Each of the ridges 314 has a generally convex shape that can facilitate increasing traction or gripping of the patient's finger to the finger bed. Advantageously, the ridges 314 can improve the accuracy of spectroscopic analysis in certain embodiments by reducing noise that can result from a measurement site moving or shaking loose inside of the sensor 301a. The ridges 314 can be made from reflective or opaque materials in some embodiments to further increase SNR. In other implementations, other surface shapes can be used, such as, for example, generally flat, concave, or convex finger beds 310.

[0107] Finger bed 310 can also include an embodiment of a tissue thickness adjuster or protrusion 305. The protrusion 305 includes a measurement site contact area 370 (see FIGURE 3C) that can contact body tissue of a measurement site. The protrusion 305 can be removed from or integrated with the finger bed 310. Interchangeable, different shaped protrusions 305 can also be provided, which can correspond to different finger shapes, characteristics, opacity, sizes, or the like.

[0108] Referring specifically to **FIGURE 3C**, the contact area 370 of the protrusion 305 can include openings or windows 320, 321, 322, and 323. When light from a measurement site passes through the windows 320, 321, 322, and 323, the light can reach one or more photodetectors (see FIGURE 3E). In an embodiment, the windows 320, 321, 322, and 323 mirror specific detector placements layouts such that light can impinge through the protrusion 305 onto the photodetectors. Any number of windows 320, 321, 322, and 323 can be employed in the protrusion 305 to allow light to pass from the measurement site to the photodetectors.

[0109] The windows 320, 321, 322, and 323 can also include shielding, such as an embedded grid of wiring or a conductive glass coating, to reduce noise from ambient light or other electromagnetic noise. The windows 320, 321, 322, and 323 can be made from materials, such as plastic or glass. In some embodiments, the windows 320, 321, 322, and 323 can be constructed from conductive glass, such as indium tin oxide (ITO) coated glass. Conductive glass can be useful because its shielding is transparent, and thus allows for a larger aperture versus a window with an embedded grid of wiring. In addition, in certain embodiments, the conductive glass does not need openings in its shielding (since it is transparent), which enhances its shielding performance. For example, some embodiments that employ the conductive glass can attain up to an about 40% to about 50% greater signal than non-conductive glass with a shielding grid. In addition, in some embodiments, conductive glass can be useful for shielding noise from a greater variety of directions than non-conductive glass with a shielding grid.

[0110] Turning to **FIGURE 3B**, the sensor 301a can also include a shielding 315a, such as a metal cage, box, metal sheet, perforated metal sheet, a metal layer on a non-metal material, or the like. The shielding 315a is provided in the depicted embodiment below or embedded within the protrusion 305 to reduce noise. The shielding 315a can be constructed from a conductive material, such as copper. The shielding 315a can include one or more openings or windows (not shown). The windows can be made from glass or plastic to thereby allow light that has passed through the windows 320, 321, 322, and 323 on an external surface of the protrusion 305 (see **FIGURE 3C**) to pass through to one or more photodetectors that can be enclosed or provided below (see **FIGURE 3E**).

[0111] In some embodiments, the shielding cage for shielding 315a can be constructed in a single manufactured component with or without the use of conductive glass. This form of construction may be useful in order to reduce costs of manufacture as well as assist in quality control of the components. Furthermore, the shielding cage can also be used to house various other components, such as sigma delta components for various embodiments of front end interfaces 108.

[0112] In an embodiment, the photodetectors can be positioned within or directly beneath the protrusion 305 (see **FIGURE 3E**). In such cases, the mean optical path length from the emitters to the detectors can be reduced and the accuracy of blood analyte measurement can increase. For example, in one embodiment, a convex bump of about 1 mm to about 3 mm in height and about 10 mm<sup>2</sup> to about 60 mm<sup>2</sup> was found to help signal strength by about an order of magnitude versus other shapes. Of course other dimensions and sizes can be employed in other embodiments. Depending on the properties desired, the length, width, and height of the protrusion 305 can be selected. In making such determinations, consideration can be made of protrusion's 305 effect on blood flow at the measurement site and mean path length for optical radiation passing through openings 320, 321, 322, and 323. Patient comfort can also be considered in determining the size and shape of the protrusion.

[0113] In an embodiment, the protrusion 305 can include a pliant material, including soft plastic or rubber, which can somewhat conform to the shape of a

measurement site. Pliant materials can improve patient comfort and tactility by conforming the measurement site contact area 370 to the measurement site. Additionally, pliant materials can minimize or reduce noise, such as ambient light. Alternatively, the protrusion 305 can be made from a rigid material, such as hard plastic or metal.

**[0114]** Rigid materials can improve measurement accuracy of a blood analyte by conforming the measurement site to the contact area 370. The contact area 370 can be an ideal shape for improving accuracy or reducing noise. Selecting a material for the protrusion 305 can include consideration of materials that do not significantly alter blood flow at the measurement site. The protrusion 305 and the contact area 370 can include a combination of materials with various characteristics.

**[0115]** The contact area 370 serves as a contact surface for the measurement site. For example, in some embodiments, the contact area 370 can be shaped for contact with a patient's finger. Accordingly, the contact area 370 can be sized and shaped for different sizes of fingers. The contact area 370 can be constructed of different materials for reflective purposes as well as for the comfort of the patient. For example, the contact area 370 can be constructed from materials having various hardness and textures, such as plastic, gel, foam, and the like.

**[0116]** The formulas and analysis that follow with respect to **FIGURE 5** provide insight into how selecting these variables can alter transmittance and intensity gain of optical radiation that has been applied to the measurement site. These examples do not limit the scope of this disclosure.

**[0117]** Referring to **FIGURE 5**, a plot 500 is shown that illustrates examples of effects of embodiments of the protrusion 305 on the SNR at various wavelengths of light. As described above, the protrusion 305 can assist in conforming the tissue and effectively reduce its mean path length. In some instances, this effect by the protrusion 305 can have significant impact on increasing the SNR.

**[0118]** According to the Beer Lambert law, a transmittance of light ( $I$ ) can be expressed as follows:  $I = I_0 * e^{-m*b*c}$ , where  $I_0$  is the initial power of light being transmitted,  $m$  is the path length traveled by the light, and the component " $b*c$ "

corresponds to the bulk absorption of the light at a specific wavelength of light. For light at about 1600 nm to about 1700 nm, for example, the bulk absorption component is generally around  $0.7 \text{ mm}^{-1}$ . Assuming a typical finger thickness of about 12 mm and a mean path length of 20 mm due to tissue scattering, then  $I = I_0 * e^{(-20*0.7)}$ .

**[0119]** In an embodiment where the protrusion 305 is a convex bump, the thickness of the finger can be reduced to 10 mm (from 12 mm) for some fingers and the effective light mean path is reduced to about 16.6 mm from 20 mm (see box 510). This results in a new transmittance,  $I_1 = I_0 * e^{(-16.6*0.7)}$ . A curve for a typical finger (having a mean path length of 20 mm) across various wavelengths is shown in the plot 500 of **FIGURE 5**. The plot 500 illustrates potential effects of the protrusion 305 on the transmittance. As illustrated, comparing  $I$  and  $I_1$  results in an intensity gain of  $e^{(-16.6*0.7)}/e^{(-20*0.7)}$ , which is about a 10 times increase for light in the about 1600 nm to about 1700 nm range. Such an increase can affect the SNR at which the sensor can operate. The foregoing gains can be due at least in part to the about 1600 nm to about 1700 nm range having high values in bulk absorptions (water, protein, and the like), e.g., about  $0.7 \text{ mm}^{-1}$ . The plot 500 also shows improvements in the visible/near-infrared range (about 600 nm to about 1300 nm).

**[0120]** Turning again to **FIGURES 3A** through **3C**, an example heat sink 350a is also shown. The heat sink 350a can be attached to, or protrude from an outer surface of, the sensor 301a, thereby providing increased ability for various sensor components to dissipate excess heat. By being on the outer surface of the sensor 301a in certain embodiments, the heat sink 350a can be exposed to the air and thereby facilitate more efficient cooling. In an embodiment, one or more of the emitters (see **FIGURE 1**) generate sufficient heat that inclusion of the heat sink 350a can advantageously allows the sensor 301a to remain safely cooled. The heat sink 350a can include one or more materials that help dissipate heat, such as, for example, aluminum, steel, copper, carbon, combinations of the same, or the like. For example, in some embodiments, the emitter shell 304a can include a heat conducting material that is also readily and relatively inexpensively moldable into desired shapes and forms.



**[0121]** In some embodiments, the heat sink 350a includes metalicized plastic. The metalicized plastic can include aluminum and carbon, for example. The material can allow for improved thermal conductivity and diffusivity, which can increase commercial viability of the heat sink. In some embodiments, the material selected to construct the heat sink 350a can include a thermally conductive liquid crystalline polymer, such as CoolPoly<sup>®</sup> D5506, commercially available from Cool Polymers<sup>®</sup>, Inc. of Warwick, Rhode Island. Such a material can be selected for its electrically non-conductive and dielectric properties so as, for example, to aid in electrical shielding. In an embodiment, the heat sink 350a provides improved heat transfer properties when the sensor 301a is active for short intervals of less than a full day's use. In an embodiment, the heat sink 350a can advantageously provide improved heat transfers in about three (3) to about four (4) minute intervals, for example, although a heat sink 350a can be selected that performs effectively in shorter or longer intervals.

**[0122]** Moreover, the heat sink 350a can have different shapes and configurations for aesthetic as well as for functional purposes. In an embodiment, the heat sink is configured to maximize heat dissipation, for example, by maximizing surface area. In an embodiment, the heat sink 350a is molded into a generally curved surface and includes one or more fins, undulations, grooves, or channels. The example heat sink 350a shown includes fins 351a (see FIGURE 3A).

**[0123]** An alternative shape of a sensor 301b and heat sink 350b is shown in **FIGURE 3D**. The sensor 301b can include some or all of the features of the sensor 301a. For example, the sensor 301b includes an enclosure 302b formed by an emitter shell 304b and a detector shell 306b, pivotably connected about a pivot 303a. The emitter shell 304b can also include absorbing opaque material on one or more flaps 307b, and the detector shell 306a can also include absorbing opaque material at various areas, such as lower area 308b.

**[0124]** However, the shape of the sensor 301b is different in this embodiment. In particular, the heat sink 350b includes comb protrusions 351b. The comb protrusions 351b are exposed to the air in a similar manner to the fins 351a of the heat sink 350a, thereby facilitating efficient cooling of the sensor 301b.

**[0125]** **FIGURE 3E** illustrates a more detailed example of a detector shell 306b of the sensor 301b. The features described with respect to the detector shell 306b can also be used with the detector shell 306a of the sensor 301a.

**[0126]** As shown, the detector shell 306b includes detectors 316. The detectors 316 can have a predetermined spacing 340 from each other, or a spatial relationship among one another that results in a spatial configuration. This spatial configuration can purposefully create a variation of path lengths among detectors 316 and the emitter discussed above.

**[0127]** In the depicted embodiment, the detector shell 316 can hold multiple (e.g., two, three, four, etc.) photodiode arrays that are arranged in a two-dimensional grid pattern. Multiple photodiode arrays can also be useful to detect light piping (e.g., light that bypasses measurement site 102). In the detector shell 316, walls can be provided to separate the individual photodiode arrays to prevent or reduce mixing of light signals from distinct quadrants. In addition, the detector shell 316 can be covered by windows of transparent material, such as glass, plastic, or the like, to allow maximum or increased transmission of power light captured. In various embodiments, the transparent materials used can also be partially transparent or translucent or can otherwise pass some or all of the optical radiation passing through them. As noted, this window can include some shielding in the form of an embedded grid of wiring, or a conductive layer or coating.

**[0128]** As further illustrated by **FIGURE 3E**, the detectors 316 can have a spatial configuration of a grid. However, the detectors 316 can be arranged in other configurations that vary the path length. For example, the detectors 316 can be arranged in a linear array, a logarithmic array, a two-dimensional array, a zig-zag pattern, or the like. Furthermore, any number of the detectors 316 can be employed in certain embodiments.

**[0129]** **FIGURE 3F** illustrates another embodiment of a sensor 301f. The sensor 301f can include some or all of the features of the sensor 301a of **FIGURE 3A** described above. For example, the sensor 301f includes an enclosure 302f formed by an upper section or emitter shell 304f, which is pivotably connected with a lower section or detector shell 306f around a pivot point 303f. The emitter shell 304f

can also include absorbing opaque material on various areas, such as on one or more flaps 307f, to reduce ambient light entering the sensor 301f. The detector shell 306f can also include absorbing opaque material at various areas, such as a lower area 308f. The sensor 301f also includes a heat sink 350f, which includes fins 351f.

**[0130]** In addition to these features, the sensor 301f includes a flex circuit cover 360, which can be made of plastic or another suitable material. The flex circuit cover 360 can cover and thereby protect a flex circuit (not shown) that extends from the emitter shell 304f to the detector shell 306f. An example of such a flex circuit is illustrated in U.S. Publication No. 2006/0211924, incorporated above (see FIGURE 46 and associated description, which is hereby specifically incorporated by reference). The flex circuit cover 360 is shown in more detail below in FIGURE 17.

**[0131]** In addition, sensors 301a-f has extra length – extends to second joint on finger - Easier to place, harder to move due to cable, better for light piping

**[0132]** **FIGURES 4A through 4C** illustrate example arrangements of a protrusion 405, which is an embodiment of the protrusion 305 described above. In an embodiment, the protrusion 405 can include a measurement site contact area 470. The measurement site contact area 470 can include a surface that molds body tissue of a measurement site, such as a finger, into a flat or relatively flat surface.

**[0133]** The protrusion 405 can have dimensions that are suitable for a measurement site such as a patient's finger. As shown, the protrusion 405 can have a length 400, a width 410, and a height 430. The length 400 can be from about 9 to about 11 millimeters, e.g., about 10 millimeters. The width 410 can be from about 7 to about 9 millimeters, e.g., about 8 millimeters. The height 430 can be from about 0.5 millimeters to about 3 millimeters, e.g., about 2 millimeters. In an embodiment, the dimensions 400, 410, and 430 can be selected such that the measurement site contact area 470 includes an area of about 80 square millimeters, although larger and smaller areas can be used for different sized tissue for an adult, an adolescent, or infant, or for other considerations.

**[0134]** The measurement site contact area 470 can also include differently shaped surfaces that conform the measurement site into different shapes. For example, the measurement site contact area 470 can be generally curved and/or convex with respect to the measurement site. The measurement site contact area 470 can be other shapes that reduce or even minimize air between the protrusion 405 and or the measurement site. Additionally, the surface pattern of the measurement site contact area 470 can vary from smooth to bumpy, e.g., to provide varying levels of grip.

**[0135]** In **FIGURES 4A** and **4C**, openings or windows 420, 421, 422, and 423 can include a wide variety of shapes and sizes, including for example, generally square, circular, triangular, or combinations thereof. The windows 420, 421, 422, and 423 can be of non-uniform shapes and sizes. As shown, the windows 420, 421, 422, and 423 can be evenly spaced out in a grid like arrangement. Other arrangements or patterns of arranging the windows 420, 421, 422, and 423 are possible. For example, the windows 420, 421, 422, and 423 can be placed in a triangular, circular, or linear arrangement. In some embodiments, the windows 420, 421, 422, and 423 can be placed at different heights with respect to the finger bed 310 of **FIGURE 3**. The windows 420, 421, 422, and 423 can also mimic or approximately mimic a configuration of, or even house, a plurality of detectors.

**[0136]** **FIGURES 6A** through **6D** illustrate another embodiment of a protrusion 605 that can be used as the tissue shaper 105 described above or in place of the protrusions 305, 405 described above. The depicted protrusion 605 is a partially cylindrical lens having a partial cylinder 608 and an extension 610. The partial cylinder 608 can be a half cylinder in some embodiments; however, a smaller or greater portion than half of a cylinder can be used. Advantageously, in certain embodiments, the partially cylindrical protrusion 605 focuses light onto a smaller area, such that fewer detectors can be used to detect the light attenuated by a measurement site.

**[0137]** **FIGURE 6A** illustrates a perspective view of the partially cylindrical protrusion 605. **FIGURE 6B** illustrates a front elevation view of the partially cylindrical protrusion 605. **FIGURE 6C** illustrates a side view of the partially

cylindrical protrusion 605. **FIGURE 6D** illustrates a top view of the partially cylindrical protrusion 605.

**[0138]** Advantageously, in certain embodiments, placing the partially cylindrical protrusion 605 over the photodiodes in any of the sensors described above adds multiple benefits to any of the sensors described above. In one embodiment, the partially cylindrical protrusion 605 penetrates into the tissue and reduces the path length of the light traveling in the tissue, similar to the protrusions described above.

**[0139]** The partially cylindrical protrusion 605 can also collect light from a large surface and focus down the light to a smaller area. As a result, in certain embodiments, signal strength per area of the photodiode can be increased. The partially cylindrical protrusion 605 can therefore facilitate a lower cost sensor because, in certain embodiments, less photodiode area can be used to obtain the same signal strength. Less photodiode area can be realized by using smaller photodiodes or fewer photodiodes (see, e.g., **FIGURE 14**). If fewer or smaller photodiodes are used, the partially cylindrical protrusion 605 can also facilitate an improved SNR of the sensor because fewer or smaller photodiodes can have less dark current.

**[0140]** The dimensions of the partially cylindrical protrusion 605 can vary based on, for instance, a number of photodiodes used with the sensor. Referring to **FIGURE 6C**, the overall height of the partially cylindrical protrusion 605 (measurement “a”) in some implementations is about 1 to about 3 mm. A height in this range can allow the partially cylindrical protrusion 605 to penetrate into the pad of the finger or other tissue and reduce the distance that light travels through the tissue. Other heights, however, of the partially cylindrical protrusion 605 can also accomplish this objective. For example, the chosen height of the partially cylindrical protrusion 605 can be selected based on the size of the measurement site, whether the patient is an adult or child, and so on. In an embodiment, the height of the protrusion 605 is chosen to provide as much tissue thickness reduction as possible while reducing or preventing occlusion of blood vessels in the tissue.

[0141] Referring to **FIGURE 6D**, the width of the partially cylindrical protrusion 605 (measurement “b”) can be about 3 to about 5 mm. In one embodiment, the width is about 4 mm. In one embodiment, a width in this range provides good penetration of the partially cylindrical protrusion 605 into the tissue to reduce the path length of the light. Other widths, however, of the partially cylindrical protrusion 605 can also accomplish this objective. For example, the width of the partially cylindrical protrusion 605 can vary based on the size of the measurement site, whether the patient is an adult or child, and so on. In addition, the length of the protrusion 605 could be about 10 mm, or about 8 mm to about 12 mm, or smaller than 8 mm or greater than 12 mm.

[0142] In certain embodiments, the focal length ( $f$ ) for the partially cylindrical protrusion 605 can be expressed as:  $f = \frac{R}{n-1}$ , where  $R$  is the radius of curvature of the partial cylinder 608 and  $n$  is the index of refraction of the material used. In certain embodiments, the radius of curvature can be between about 1.5 mm and about 2 mm. In another embodiment, the partially cylindrical protrusion 605 can include a material, such as nBK7 glass, with an index of refraction of around 1.5 at 1300 nm, which can provide focal lengths of between about 3 mm and about 4 mm.

[0143] A partially cylindrical protrusion 605 having a material with a higher index of refraction such as nSF11 glass (e.g.,  $n=1.75$  at 1300 nm) can provide a shorter focal length and possibly a smaller photodiode chip, but can also cause higher reflections due to the index of refraction mismatch with air. Many types of glass or plastic can be used with index of refraction values ranging from, for example, about 1.4 to about 1.9. The index of refraction of the material of the protrusion 605 can be chosen to improve or optimize the light focusing properties of the protrusion 605. A plastic partially cylindrical protrusion 605 could provide the cheapest option in high volumes but can also have some undesired light absorption peaks at wavelengths higher than 1500 nm. Other focal lengths and materials having different indices of refraction can be used for the partially cylindrical protrusion 605.

**[0144]** Placing a photodiode at a given distance below the partially cylindrical protrusion 605 can facilitate capturing some or all of the light traveling perpendicular to the lens within the active area of the photodiode (see FIGURE 14). Different sizes of the partially cylindrical protrusion 605 can use different sizes of photodiodes. The extension 610 added onto the bottom of the partial cylinder 608 is used in certain embodiments to increase the height of the partially cylindrical protrusion 605. In an embodiment, the added height is such that the photodiodes are at or are approximately at the focal length of the partially cylindrical protrusion 605. In an embodiment, the added height provides for greater thinning of the measurement site. In an embodiment, the added height assists in deflecting light piped through the sensor. This is because light piped around the sensor passes through the side walls of the added height without being directed toward the detectors. The extension 610 can also further facilitate the protrusion 605 increasing or maximizing the amount of light that is provided to the detectors. In some embodiments, the extension 610 can be omitted.

**[0145]** FIGURE 6E illustrates another view of the sensor 301f of FIGURE 3F, which includes an embodiment of a partially cylindrical protrusion 605b. Like the sensor 301A shown in FIGURES 3B and 3C, the sensor 301f includes a finger bed 310f. The finger bed 310f includes a generally curved surface shaped generally to receive tissue, such as a human digit. The finger bed 310f also includes the ridges or channels 314 described above with respect to FIGURES 3B and 3C.

**[0146]** The example of finger bed 310f shown also includes the protrusion 605b, which includes the features of the protrusion 605 described above. In addition, the protrusion 605b also includes chamfered edges 607 on each end to provide a more comfortable surface for a finger to slide across (see also FIGURE 14D). In another embodiment, the protrusion 605b could instead include a single chamfered edge 607 proximal to the ridges 314. In another embodiment, one or both of the chamfered edges 607 could be rounded.

**[0147]** The protrusion 605b also includes a measurement site contact area 670 that can contact body tissue of a measurement site. The protrusion 605b can be removed from or integrated with the finger bed 310f. Interchangeable, differently

shaped protrusions 605b can also be provided, which can correspond to different finger shapes, characteristics, opacity, sizes, or the like.

**[0148]** **FIGURES 7A** and **7B** illustrate block diagrams of sensors 701 that include example arrangements of conductive glass or conductive coated glass for shielding. Advantageously, in certain embodiments, the shielding can provide increased SNR. The features of the sensors 701 can be implemented with any of the sensors 101, 201, 301 described above. Although not shown, the partially cylindrical protrusion 605 of **FIGURE 6** can also be used with the sensors 701 in certain embodiments.

**[0149]** For example, referring specifically to **FIGURE 7A**, the sensor 701a includes an emitter housing 704a and a detector housing 706. The emitter housing 704a includes LEDs 104. The detector housing 706a includes a tissue bed 710a with an opening or window 703a, the conductive glass 730a, and one or more photodiodes for detectors 106 provided on a submount 707a.

**[0150]** During operation, a finger 102 can be placed on the tissue bed 710a and optical radiation can be emitted from the LEDs 104. Light can then be attenuated as it passes through or is reflected from the tissue of the finger 102. The attenuated light can then pass through the opening 703a in the tissue bed 710a. Based on the received light, the detectors 106 can provide a detector signal 107, for example, to the front end interface 108 (see **FIGURE 1**).

**[0151]** In the depicted embodiment, the conductive glass 730 is provided in the opening 703. The conductive glass 730 can thus not only permit light from the finger to pass to the detectors 106, but it can also supplement the shielding of the detectors 106 from noise. The conductive glass 730 can include a stack or set of layers. In **FIGURE 7A**, the conductive glass 730a is shown having a glass layer 731 proximate the finger 102 and a conductive layer 733 electrically coupled to the shielding 790a.

**[0152]** In an embodiment, the conductive glass 730a can be coated with a conductive, transparent or partially transparent material, such as a thin film of indium tin oxide (ITO). To supplement electrical shielding effects of a shielding enclosure 790a, the conductive glass 730a can be electrically coupled to the



shielding enclosure 790a. The conductive glass 730a can be electrically coupled to the shielding 704a based on direct contact or via other connection devices, such as a wire or another component.

**[0153]** The shielding enclosure 790a can be provided to encompass the detectors 106 to reduce or prevent noise. For example, the shielding enclosure 790a can be constructed from a conductive material, such as copper, in the form of a metal cage. The shielding or enclosure a can include an opaque material to not only reduce electrical noise, but also ambient optical noise.

**[0154]** In some embodiments, the shielding enclosure 790a can be constructed in a single manufactured component with or without the use of conductive glass. This form of construction may be useful in order to reduce costs of manufacture as well as assist in quality control of the components. Furthermore, the shielding enclosure 790a can also be used to house various other components, such as sigma delta components for various embodiments of front end interfaces 108.

**[0155]** Referring to **FIGURE 7B**, another block diagram of an example sensor 701b is shown. A tissue bed 710b of the sensor 701b includes a protrusion 705b, which is in the form of a convex bump. The protrusion 705b can include all of the features of the protrusions or tissue shaping materials described above. For example, the protrusion 705b includes a contact area 370 that comes in contact with the finger 102 and which can include one or more openings 703b. One or more components of conductive glass 730b can be provided in the openings 703. For example, in an embodiment, each of the openings 703 can include a separate window of the conductive glass 730b. In an embodiment, a single piece of the conductive glass 730b can be used for some or all of the openings 703b. The conductive glass 730b is smaller than the conductive glass 730a in this particular embodiment.

**[0156]** A shielding enclosure 790b is also provided, which can have all the features of the shielding enclosure 790a. The shielding enclosure 790b is smaller than the shielding enclosure 790a; however, a variety of sizes can be selected for the shielding enclosures 790.

**[0157]** In some embodiments, the shielding enclosure 790b can be constructed in a single manufactured component with or without the use of conductive glass. This form of construction may be useful in order to reduce costs of manufacture as well as assist in quality control of the components. Furthermore, the shielding enclosure 790b can also be used to house various other components, such as sigma delta components for various embodiments of front end interfaces 108.

**[0158]** **FIGURES 8A** through **8D** illustrate a perspective view, side views, and a bottom elevation view of the conductive glass described above with respect to the sensors 701a, 701b. As shown in the perspective view of **FIGURE 8A** and side view of **FIGURE 8B**, the conductive glass 730 includes the electrically conductive material 733 described above as a coating on the glass layer 731 described above to form a stack. In an embodiment where the electrically conductive material 733 includes indium tin oxide, surface resistivity of the electrically conductive material 733 can range approximately from 30 ohms per square inch to 500 ohms per square inch, or approximately 30, 200, or 500 ohms per square inch. As would be understood by a person of skill in the art from the present disclosure, other resistivities can also be used which are less than 30 ohms or more than 500 ohms. Other transparent, electrically conductive materials can be used as the material 733.

**[0159]** Although the conductive material 733 is shown spread over the surface of the glass layer 731, the conductive material 733 can be patterned or provided on selected portions of the glass layer 731. Furthermore, the conductive material 733 can have uniform or varying thickness depending on a desired transmission of light, a desired shielding effect, and other considerations.

**[0160]** In **FIGURE 8C**, a side view of a conductive glass 830a is shown to illustrate an embodiment where the electrically conductive material 733 is provided as an internal layer between two glass layers 731, 835. Various combinations of integrating electrically conductive material 733 with glass are possible. For example, the electrically conductive material 733 can be a layer within a stack of layers. This stack of layers can include one or more layers of glass 731, 835, as

well as one or more layers of conductive material 733. The stack can include other layers of materials to achieve desired characteristics.

**[0161]** In **FIGURE 8D**, a bottom perspective view is shown to illustrate an embodiment where a conductive glass 830b can include conductive material 837 that occupies or covers a portion of a glass layer 839. This embodiment can be useful, for example, to create individual, shielded windows for detectors 106, such as those shown in **FIGURE 3C**. The conductive material 837 can be patterned to include an area 838 to allow light to pass to detectors 106 and one or more strips 841 to couple to the shielding 704 of **FIGURE 7**.

**[0162]** Other configurations and patterns for the conductive material can be used in certain embodiments, such as, for example, a conductive coating lining periphery edges, a conductive coating outlaid in a pattern including a grid or other pattern, a speckled conductive coating, coating outlaid in lines in either direction or diagonally, varied thicknesses from the center out or from the periphery in, or other suitable patterns or coatings that balance the shielding properties with transparency considerations.

**[0163]** **FIGURE 9** depicts an example graph 900 that illustrates comparative results obtained by an example sensor having components similar to those disclosed above with respect to **FIGURES 7 and 8**. The graph 900 depicts the results of the percentage of transmission of varying wavelengths of light for different types of windows used in the sensors described above.

**[0164]** A line 915 on the graph 900 illustrates example light transmission of a window made from plain glass. As shown, the light transmission percentage of varying wavelengths of light is approximately 90% for a window made from plain glass. A line 920 on the graph 900 demonstrates an example light transmission percentage for an embodiment in which a window is made from glass having an ITO coating with a surface resistivity of 500 ohms per square inch. A line 925 on the graph 900 shows an example light transmission for an embodiment in which a window is made from glass that includes a coating of ITO oxide with a surface resistivity of 200 ohms per square inch. A line 930 on the graph 900 shows an example light transmission for an embodiment in which a window is made from

glass that includes a coating of ITO oxide with a surface resistivity of 30 ohms per square inch.

**[0165]** The light transmission percentage for a window with currently available embedded wiring can have a light transmission percentage of approximately 70%. This lower percentage of light transmission can be due to the opacity of the wiring employed in a currently available window with wiring. Accordingly, certain embodiments of glass coatings described herein can employ, for example, ITO coatings with different surface resistivity depending on the desired light transmission, wavelengths of light used for measurement, desired shielding effect, and other criteria.

**[0166]** **FIGURES 10A** through **10B** illustrate comparative noise floors of example implementations of the sensors described above. Noise can include optical noise from ambient light and electro-magnetic noise, for example, from surrounding electrical equipment. In **FIGURE 10A**, a graph 1000 depicts possible noise floors for different frequencies of noise for an embodiment in which one of the sensors described above included separate windows for four (4) detectors 106. One or more of the windows included an embedded grid of wiring as a noise shield. Symbols 1030 - 1033 illustrate the noise floor performance for this embodiment. As can be seen, the noise floor performance can vary for each of the openings and based on the frequency of the noise.

**[0167]** In **FIGURE 10B**, a graph 1050 depicts a noise floor for frequencies of noise 1070 for an embodiment in which the sensor included separate openings for four (4) detectors 106 and one or more windows that include an ITO coating. In this embodiment, a surface resistivity of the ITO used was about 500 ohms per square inch. Symbols 1080 - 1083 illustrate the noise floor performance for this embodiment. As can be seen, the noise floor performance for this embodiment can vary less for each of the openings and provide lower noise floors in comparison to the embodiment of **FIGURE 10A**.

**[0168]** **FIGURE 11A** illustrates an example structure for configuring the set of optical sources of the emitters described above. As shown, an emitter 104 can include a driver 1105, a thermistor 1120, a set of top-emitting LEDs 1102 for

emitting red and/or infrared light, a set of side-emitting LEDs 1104 for emitting near infrared light, and a submount 1106.

**[0169]** The thermistor 1120 can be provided to compensate for temperature variations. For example, the thermistor 1120 can be provided to allow for wavelength centroid and power drift of LEDs 1102 and 1104 due to heating. In addition, other thermistors (~~not shown~~) can be employed, for example, to measure a temperature of a measurement site. The temperature can be displayed on a display device and used by a caregiver. Such a temperature can also be helpful in correcting for wavelength drift due to changes in water absorption, which can be temperature dependent, thereby providing more accurate data useful in detecting blood analytes like glucose. In addition, using a thermistor or other type of temperature sensitive device may be useful for detecting extreme temperatures at the measurement site that are too hot or too cold. The presence of low perfusion may also be detected, for example, when the finger of a patient has become too cold. Moreover, shifts in temperature at the measurement site can alter the absorption spectrum of water and other tissue in the measurement cite. A thermistor's temperature reading can be used to adjust for the variations in absorption spectrum changes in the measurement site.

**[0170]** The driver 1105 can provide pulses of current to the emitter 1104. In an embodiment, the driver 1105 drives the emitter 1104 in a progressive fashion, for example, in an alternating manner based on a control signal from, for example, a processor (e.g., the processor 110). For example, the driver 1105 can drive the emitter 1104 with a series of pulses to about 1 milliwatt (mW) for visible light to light at about 1300 nm and from about 40 mW to about 100 mW for light at about 1600 nm to about 1700 nm. However, a wide number of driving powers and driving methodologies can be used. The driver 1105 can be synchronized with other parts of the sensor and can minimize or reduce any jitter in the timing of pulses of optical radiation emitted from the emitter 1104. In some embodiments, the driver 1105 is capable of driving the emitter 1104 to emit an optical radiation in a pattern that varies by less than about 10 parts-per-million; however other amounts of variation can be used.

[0171] The submount 1106 provides a support structure in certain embodiments for aligning the top-emitting LEDs 1102 and the side-emitting LEDs 1104 so that their optical radiation is transmitted generally towards the measurement site. In some embodiments, the submount 1106 is also constructed of aluminum nitride (AlN) or beryllium oxide (BEO) for heat dissipation, although other materials or combinations of materials suitable for the submount 1106 can be used.

[0172] **FIGURE 11B** illustrates a configuration of emitting optical radiation into a measurement site for measuring a blood constituent or analyte like glucose. In some embodiments, emitter 104 may be driven in a progressive fashion to minimize noise and increase SNR of sensor 101. For example, emitter 104 may be driven based on a progression of power/current delivered to LEDs 1102 and 1104.

[0173] In some embodiments, emitter 104 may be configured to emit pulses centered about 905 nm, about 1050 nm, about 1200 nm, about 1300 nm, about 1330 nm, about 1610 nm, about 1640 nm, and about 1665 nm. In another embodiment, the emitter 104 may emit optical radiation ranging from about 860 nm to about 950 nm, about 950 nm to about 1100 nm, about 1100 nm to about 1270 nm, about 1250 nm to about 1350 nm, about 1300 nm to about 1360 nm, and about 1590 nm to about 1700 nm. Of course, emitter 104 may be configured to transmit any of a variety of wavelengths of visible, or near-infrared optical radiation.

[0174] For purposes of illustration, **FIGURE 11B** shows a sequence of pulses of light at wavelengths of around 905 nm, around 1200 nm, around 1300 nm, and around 1330 nm from top emitting LEDs 1102. **FIGURE 11B** also shows that emitter 104 may then emit pulses centered at around 1630 nm, around 1660 nm, and around 1615 nm from side emitting LEDs 1104. Emitter 104 may be progressively driven at higher power/current. This progression may allow driver circuit 105 to stabilize in its operations, and thus, provide a more stable current/power to LEDs 1102 and 1104.

[0175] For example, as shown in **FIGURE 11B**, the sequence of optical radiation pulses are shown having a logarithmic-like progression in power/current. In some embodiments, the timing of these pulses is based on a cycle of about 400

slots running at 48 kHz (e.g. each time slot may be approximately 0.02 ms or 20 microseconds). An artisan will recognize that term "slots" includes its ordinary meaning, which includes a time period that may also be expressed in terms of a frequency. In the example shown, pulses from top emitting LEDs 1102 may have a pulse width of about 40 time slots (e.g., about 0.8 ms) and an off period of about 4 time slots in between. In addition, pulses from side emitting LEDs 1104 (e.g., or a laser diode) may have a pulse width of about 60 time slots (e.g., about 1.25 ms) and a similar off period of about 4 time slots. A pause of about 70 time slots (e.g. 1.5 ms) may also be provided in order to allow driver circuit 1105 to stabilize after operating at higher current/power.

**[0176]** As shown in **FIGURE 11B**, top emitting LEDs 1102 may be initially driven with a power to approximately 1 mW at a current of about 20-100 mA. Power in these LEDs may also be modulated by using a filter or covering of black dye to reduce power output of LEDs. In this example, top emitting LEDs 1102 may be driven at approximately 0.02 to 0.08 mW. The sequence of the wavelengths may be based on the current requirements of top emitting LEDs 502 for that particular wavelength. Of course, in other embodiments, different wavelengths and sequences of wavelengths may be output from emitter 104.

**[0177]** Subsequently, side emitting LEDs 1104 may be driven at higher powers, such as about 40-100 mW and higher currents of about 600-800 mA. This higher power may be employed in order to compensate for the higher opacity of tissue and water in measurement site 102 to these wavelengths. For example, as shown, pulses at about 1630 nm, about 1660 nm, and about 1615 nm may be output with progressively higher power, such as at about 40 mW, about 50 mW, and about 60 mW, respectively. In this embodiment, the order of wavelengths may be based on the optical characteristics of that wavelength in tissue as well as the current needed to drive side emitting LEDs 1104. For example, in this embodiment, the optical pulse at about 1615 nm is driven at the highest power due to its sensitivity in detecting analytes like glucose and the ability of light at this wavelength to penetrate tissue. Of course, different wavelengths and sequences of wavelengths may be output from emitter 104.

**[0178]** As noted, this progression may be useful in some embodiments because it allows the circuitry of driver circuit 1105 to stabilize its power delivery to LEDs 1102 and 1104. Driver circuit 1105 may be allowed to stabilize based on the duty cycle of the pulses or, for example, by configuring a variable waiting period to allow for stabilization of driver circuit 1105. Of course, other variations in power/current and wavelength may also be employed in the present disclosure.

**[0179]** Modulation in the duty cycle of the individual pulses may also be useful because duty cycle can affect the signal noise ratio of the system 100. That is, as the duty cycle is increased so may the signal to noise ratio.

**[0180]** Furthermore, as noted above, driver circuit 1105 may monitor temperatures of the LEDs 1102 and 1104 using the thermistor 1120 and adjust the output of LEDs 1102 and 1104 accordingly. Such a temperature may be to help sensor 101 correct for wavelength drift due to changes in water absorption, which can be temperature dependent.

**[0181]** **FIGURE 11C** illustrates another exemplary emitter that may be employed in the sensor according to an embodiment of the disclosure. As shown, the emitter 104 can include components mounted on a substrate 1108 and on submount 1106. In particular, top-emitting LEDs 1102 for emitting red and/or infrared light may be mounted on substrate 1108. Side emitting LEDs 1104 may be mounted on submount 1106. As noted, side-emitting LEDs 1104 may be included in emitter 104 for emitting near infrared light.

**[0182]** As also shown, the sensor of **FIGURE 11C** may include a thermistor 1120. As noted, the thermistor 1120 can be provided to compensate for temperature variations. The thermistor 1120 can be provided to allow for wavelength centroid and power drift of LEDs 1102 and 1104 due to heating. In addition, other thermistors (not shown) can be employed, for example, to measure a temperature of a measurement site. Such a temperature can be helpful in correcting for wavelength drift due to changes in water absorption, which can be temperature dependent, thereby providing more accurate data useful in detecting blood analytes like glucose.



**[0183]** In some embodiments, the emitter 104 may be implemented without the use of side emitting LEDs. For example, certain blood constituents, such as total hemoglobin, can be measured by embodiments of the disclosure without the use of side emitting LEDs. **FIGURE 11D** illustrates another exemplary emitter that may be employed in the sensor according to an embodiment of the disclosure. In particular, an emitter 104 that is configured for a blood constituent, such as total hemoglobin, is shown. The emitter 104 can include components mounted on a substrate 1108. In particular, top-emitting LEDs 1102 for emitting red and/or infrared light may be mounted on substrate 1108.

**[0184]** As also shown, the emitter of **FIGURE 11D** may include a thermistor 1120. The thermistor 1120 can be provided to compensate for temperature variations. The thermistor 1120 can be provided to allow for wavelength centroid and power drift of LEDs 1102 due to heating.

**[0185]** **FIGURE 12A** illustrates a detector submount 1200 having photodiode detectors that are arranged in a grid pattern on the detector submount 1200 to capture light at different quadrants from a measurement site. One detector submount 1200 can be placed under each window of the sensors described above, or multiple windows can be placed over a single detector submount 1200. The detector submount 1200 can also be used with the partially cylindrical protrusion 605 described above with respect to **FIGURE 6**.

**[0186]** The detectors include photodiode detectors 1-4 that are arranged in a grid pattern on the submount 1200 to capture light at different quadrants from the measurement site. As noted, other patterns of photodiodes, such as a linear row, or logarithmic row, can also be employed in certain embodiments.

**[0187]** As shown, the detectors 1-4 may have a predetermined spacing from each other, or spatial relationship among one another that result in a spatial configuration. This spatial configuration can be configured to purposefully create a variation of path lengths among detectors 106 and the point light source discussed above.

**[0188]** Detectors may hold multiple (e.g., two, three, four, etc.) photodiode arrays that are arranged in a two-dimensional grid pattern. Multiple photodiode

arrays may also be useful to detect light piping (i.e., light that bypasses measurement site 102). As shown, walls may separate the individual photodiode arrays to prevent mixing of light signals from distinct quadrants. In addition, as noted, the detectors may be covered by windows of transparent material, such as glass, plastic, etc., to allow maximum transmission of power light captured. As noted, this window may comprise some shielding in the form of an embedded grid of wiring, or a conductive layer or coating.

**[0189] FIGURES 12B through 12D** illustrate a simplified view of exemplary arrangements and spatial configurations of photodiodes for detectors 106. As shown, detectors 106 may comprise photodiode detectors 1-4 that are arranged in a grid pattern on detector submount 1200 to capture light at different quadrants from measurement site 102.

**[0190]** As noted, other patterns of photodiodes may also be employed in embodiments of the present disclosure, including, for example, stacked or other configurations recognizable to an artisan from the disclosure herein. For example, detectors 106 may be arranged in a linear array, a logarithmic array, a two-dimensional array, and the like. Furthermore, an artisan will recognize from the disclosure herein that any number of detectors 106 may be employed by embodiments of the present disclosure.

**[0191]** For example, as shown in **FIGURE 12B**, detectors 106 may comprise photodiode detectors 1-4 that are arranged in a substantially linear configuration on submount 1200. In this embodiment shown, photodiode detectors 1-4 are substantially equally spaced apart (e.g., where the distance  $D$  is substantially the same between detectors 1-4).

**[0192]** In **FIGURE 12C**, photodiode detectors 1-4 may be arranged in a substantially linear configuration on submount 1200, but may employ a substantially progressive, substantially logarithmic, or substantially semi-logarithmic spacing (e.g., where distances  $D1 > D2 > D3$ ). This arrangement or pattern may be useful for use on a patient's finger and where the thickness of the finger gradually increases.

**[0193]** In **FIGURE 12D**, a different substantially grid pattern on submount 1200 of photodiode detectors 1-4 is shown. As noted, other patterns of detectors may also be employed in embodiments of the present invention.

**[0194]** **FIGURES 12E through 12H** illustrate several embodiments of photodiodes that may be used in detectors 106. As shown in these figures, a photodiode 1202 of detector 106 may comprise a plurality of active areas 1204. These active areas 204 may be coupled together via a common cathode 1206 or anode 1208 in order to provide a larger effective detection area.

**[0195]** In particular, as shown in **FIGURE 12E**, photodiode 1202 may comprise two (2) active areas 1204a and 1204b. In **FIGURE 12F**, photodiode 1202 may comprise four (4) active areas 1204c-f. In **FIGURE 12G**, photodiode 1202 may comprise three (3) active areas 1204g-i. In **FIGURE 12H**, photodiode 1202 may comprise nine (9) active areas 1204j-r. The use of smaller active areas may be useful because smaller active areas can be easier to fabricate and can be fabricated with higher purity. However, one skilled in the art will recognize that various sizes of active areas may be employed in the photodiode 1202.

**[0196]** **FIGURE 13** illustrates an example multi-stream process 1300. The multi-stream process 1300 can be implemented by the data collection system 100 and/or by any of the sensors described above. As shown, a control signal from a signal processor 1310 controls a driver 1305. In response, an emitter 1304 generates a pulse sequence 1303 from its emitter (e.g., its LEDs) into a measurement site or sites 1302. As described above, in some embodiments, the pulse sequence 1303 is controlled to have a variation of about 10 parts per million or less. Of course, depending on the analyte desired, the tolerated variation in the pulse sequence 1303 can be greater (or smaller).

**[0197]** In response to the pulse sequence 1300, detectors 1 to n (n being an integer) in a detector 1306 capture optical radiation from the measurement site 1302 and provide respective streams of output signals. Each signal from one of detectors 1-n can be considered a stream having respective time slots corresponding to the optical pulses from emitter sets 1-n in the emitter 1304.

Although  $n$  emitters and  $n$  detectors are shown, the number of emitters and detectors need not be the same in certain implementations.

**[0198]** A front end interface 1308 can accept these multiple streams from detectors 1- $n$  and deliver one or more signals or composite signal(s) back to the signal processor 1310. A stream from the detectors 1- $n$  can thus include measured light intensities corresponding to the light pulses emitted from the emitter 1304.

**[0199]** The signal processor 1310 can then perform various calculations to measure the amount of glucose and other analytes based on these multiple streams of signals. In order to help explain how the signal processor 1310 can measure analytes like glucose, a primer on the spectroscopy employed in these embodiments will now be provided.

**[0200]** Spectroscopy is premised upon the Beer-Lambert law. According to this law, the properties of a material, e.g., glucose present in a measurement site, can be deterministically calculated from the absorption of light traveling through the material. Specifically, there is a logarithmic relation between the transmission of light through a material and the concentration of a substance and also between the transmission and the length of the path traveled by the light. As noted, this relation is known as the Beer-Lambert law.

**[0201]** The Beer-Lambert law is usually written as:

**[0202]** Absorbance  $A = m \cdot b \cdot c$ , where:

**[0203]**  $m$  is the wavelength-dependent molar absorptivity coefficient (usually expressed in units of  $M^{-1} \text{ cm}^{-1}$ );

**[0204]**  $b$  is the mean path length; and

**[0205]**  $c$  is the analyte concentration (e.g., the desired parameter).

**[0206]** In spectroscopy, instruments attempt to obtain the analyte concentration ( $c$ ) by relating absorbance ( $A$ ) to transmittance ( $T$ ). Transmittance is a proportional value defined as:

**[0207]**  $T = I / I_0$ , where:

**[0208]**  $I$  is the light intensity measured by the instrument from the measurement site; and

**[0209]**  $I_0$  is the initial light intensity from the emitter.

**[0210]** Absorbance (A) can be equated to the transmittance (T) by the equation:

**[0211]**  $A = -\log T$

**[0212]** Therefore, substituting equations from above:

**[0213]**  $A = -\log (I / I_0)$

**[0214]** In view of this relationship, spectroscopy thus relies on a proportional-based calculation of  $-\log(I / I_0)$  and solving for analyte concentration (c).

**[0215]** Typically, in order to simplify the calculations, spectroscopy will use detectors that are at the same location in order to keep the path length (b) a fixed, known constant. In addition, spectroscopy will employ various mechanisms to definitively know the transmission power ( $I_0$ ), such as a photodiode located at the light source. This architecture can be viewed as a single channel or single stream sensor, because the detectors are at a single location.

**[0216]** However, this scheme can encounter several difficulties in measuring analytes, such as glucose. This can be due to the high overlap of absorption of light by water at the wavelengths relevant to glucose as well as other factors, such as high self-noise of the components.

**[0217]** Embodiments of the present disclosure can employ a different approach that in part allows for the measurement of analytes like glucose. Some embodiments can employ a bulk, non-pulsatile measurement in order to confirm or validate a pulsatile measurement. In addition, both the non-pulsatile and pulsatile measurements can employ, among other things, the multi-stream operation described above in order to attain sufficient SNR. In particular, a single light source having multiple emitters can be used to transmit light to multiple detectors having a spatial configuration.

**[0218]** A single light source having multiple emitters can allow for a range of wavelengths of light to be used. For example, visible, infrared, and near infrared wavelengths can be employed. Varying powers of light intensity for different wavelengths can also be employed.

**[0219]** Secondly, the use of multiple-detectors in a spatial configuration allow for a bulk measurement to confirm or validate that the sensor is positioned

correctly. This is because the multiple locations of the spatial configuration can provide, for example, topology information that indicates where the sensor has been positioned. Currently available sensors do not provide such information. For example, if the bulk measurement is within a predetermined range of values, then this can indicate that the sensor is positioned correctly in order to perform pulsatile measurements for analytes like glucose. If the bulk measurement is outside of a certain range or is an unexpected value, then this can indicate that the sensor should be adjusted, or that the pulsatile measurements can be processed differently to compensate, such as using a different calibration curve or adjusting a calibration curve. This feature and others allow the embodiments to achieve noise cancellation and noise reduction, which can be several times greater in magnitude than what is achievable by currently available technology.

**[0220]** In order to help illustrate aspects of the multi-stream measurement approach, the following example derivation is provided. Transmittance (T) can be expressed as:

**[0221]**  $T = e^{-m*b*c}$

**[0222]** In terms of light intensity, this equation can also be rewritten as:

**[0223]**  $I / I_0 = e^{-m*b*c}$

**[0224]** Or, at a detector, the measured light (I) can be expressed as:

**[0225]**  $I = I_0 * e^{-m*b*c}$

**[0226]** As noted, in the present disclosure, multiple detectors (1 to n) can be employed, which results in  $I_1 \dots I_n$  streams of measurements. Assuming each of these detectors have their own path lengths,  $b_1 \dots b_n$ , from the light source, the measured light intensities can be expressed as:

**[0227]**  $I_n = I_0 * e^{-m*b_n*c}$

**[0228]** The measured light intensities at any two different detectors can be referenced to each other. For example:

**[0229]**  $I_1/I_n = (I_0 * e^{-mb_1c}) / (I_0 * e^{-mb_nc})$

**[0230]** As can be seen, the terms,  $I_0$ , cancel out and, based on exponent algebra, the equation can be rewritten as:

**[0231]**  $I_1/I_n = e^{-m(b_1-b_n)c}$

**[0232]** From this equation, the analyte concentration (c) can now be derived from bulk signals  $I_1 \dots I_n$  and knowing the respective mean path lengths  $b_1$  and  $b_n$ . This scheme also allows for the cancelling out of  $I_0$ , and thus, noise generated by the emitter 1304 can be cancelled out or reduced. In addition, since the scheme employs a mean path length difference, any changes in mean path length and topological variations from patient to patient are easily accounted. Furthermore, this bulk-measurement scheme can be extended across multiple wavelengths. This flexibility and other features allow embodiments of the present disclosure to measure blood analytes like glucose.

**[0233]** For example, as noted, the non-pulsatile, bulk measurements can be combined with pulsatile measurements to more accurately measure analytes like glucose. In particular, the non-pulsatile, bulk measurement can be used to confirm or validate the amount of glucose, protein, etc. in the pulsatile measurements taken at the tissue at the measurement site(s) 1302. The pulsatile measurements can be used to measure the amount of glucose, hemoglobin, or the like that is present in the blood. Accordingly, these different measurements can be combined to thus determine analytes like blood glucose.

**[0234]** **FIGURE 14A** illustrates an embodiment of a detector submount 1400a positioned beneath the partially cylindrical protrusion 605 of **FIGURE 6** (or alternatively, the protrusion 605b). The detector submount 1400a includes two rows 1408a of detectors 1410a. The partially cylindrical protrusion 605 can facilitate reducing the number and/or size of detectors used in a sensor because the protrusion 605 can act as a lens that focuses light onto a smaller area.

**[0235]** To illustrate, in some sensors that do not include the partially cylindrical protrusion 605, sixteen detectors can be used, including four rows of four detectors each. Multiple rows of detectors can be used to measure certain analytes, such as glucose or total hemoglobin, among others. Multiple rows of detectors can also be used to detect light piping (e.g., light that bypasses the measurement site). However, using more detectors in a sensor can add cost, complexity, and noise to the sensor.

**[0236]** Applying the partially cylindrical protrusion 605 to such a sensor, however, could reduce the number of detectors or rows of detectors used while still receiving the substantially same amount of light, due to the focusing properties of the protrusion 605 (see FIGURE 14B). This is the example situation illustrated in **FIGURE 14**—two rows 1408a of detectors 1410a are used instead of four. Advantageously, in certain embodiments, the resulting sensor can be more cost effective, have less complexity, and have an improved SNR, due to fewer and/or smaller photodiodes.

**[0237]** In other embodiments, using the partially cylindrical protrusion 605 can allow the number of detector rows to be reduced to one or three rows of four detectors. The number of detectors in each row can also be reduced. Alternatively, the number of rows might not be reduced but the size of the detectors can be reduced. Many other configurations of detector rows and sizes can also be provided.

**[0238]** **FIGURE 14B** depicts a front elevation view of the partially cylindrical protrusion 605 (or alternatively, the protrusion 605b) that illustrates how light from emitters (not shown) can be focused by the protrusion 605 onto detectors. The protrusion 605 is placed above a detector submount 1400b having one or more detectors 1410b disposed thereon. The submount 1400b can include any number of rows of detectors 1410, although one row is shown.

**[0239]** Light, represented by rays 1420, is emitted from the emitters onto the protrusion 605. These light rays 1420 can be attenuated by body tissue (not shown). When the light rays 1420 enter the protrusion 605, the protrusion 605 acts as a lens to refract the rays into rays 1422. This refraction is caused in certain embodiments by the partially cylindrical shape of the protrusion 605. The refraction causes the rays 1422 to be focused or substantially focused on the one or more detectors 1410b. Since the light is focused on a smaller area, a sensor including the protrusion 605 can include fewer detectors to capture the same amount of light compared with other sensors.

**[0240]** **FIGURE 14C** illustrates another embodiment of a detector submount 1400c, which can be disposed under the protrusion 605b (or alternatively,



the protrusion 605). The detector submount 1400c includes a single row 1408c of detectors 1410c. The detectors are electrically connected to conductors 1412c, which can be gold, silver, copper, or any other suitable conductive material.

**[0241]** The detector submount 1400c is shown positioned under the protrusion 605b in a detector subassembly 1450 illustrated in **FIGURE 14D**. A top-down view of the detector subassembly 1450 is also shown in **FIGURE 14E**. In the detector subassembly 1450, a cylindrical housing 1430 is disposed on the submount 1400c. The cylindrical housing 1430 includes a transparent cover 1432, upon which the protrusion 605b is disposed. Thus, as shown in **FIGURE 14D**, a gap 1434 exists between the detectors 1410c and the protrusion 605b. The height of this gap 1434 can be chosen to increase or maximize the amount of light that impinges on the detectors 1410c.

**[0242]** The cylindrical housing 1430 can be made of metal, plastic, or another suitable material. The transparent cover 1432 can be fabricated from glass or plastic, among other materials. The cylindrical housing 1430 can be attached to the submount 1400c at the same time or substantially the same time as the detectors 1410c to reduce manufacturing costs. A shape other than a cylinder can be selected for the housing 1430 in various embodiments.

**[0243]** In certain embodiments, the cylindrical housing 1430 (and transparent cover 1432) forms an airtight or substantially airtight or hermetic seal with the submount 1400c. As a result, the cylindrical housing 1430 can protect the detectors 1410c and conductors 1412c from fluids and vapors that can cause corrosion. Advantageously, in certain embodiments, the cylindrical housing 1430 can protect the detectors 1410c and conductors 1412c more effectively than currently-available resin epoxies, which are sometimes applied to solder joints between conductors and detectors.

**[0244]** In embodiments where the cylindrical housing 1430 is at least partially made of metal, the cylindrical housing 1430 can provide noise shielding for the detectors 1410c. For example, the cylindrical housing 1430 can be soldered to a ground connection or ground plane on the submount 1400c, which allows the cylindrical housing 1430 to reduce noise. In another embodiment, the transparent

cover 1432 can include a conductive material or conductive layer, such as conductive glass or plastic. The transparent cover 1432 can include any of the features of the noise shields 790 described above.

**[0245]** The protrusion 605b includes the chamfered edges 607 described above with respect to FIGURE 6E. These chamfered edges 607 can allow a patient to more comfortably slide a finger over the protrusion 605b when inserting the finger into the sensor 301f.

**[0246]** **FIGURE 14F** illustrates a portion of the detector shell 306f, which includes the detectors 1410c on the substrate 1400c. The substrate 1400c is enclosed by a shielding enclosure 1490, which can include the features of the shielding enclosures 790a, 790b described above (see also FIGURE 17). The shielding enclosure 1490 can be made of metal. The shielding enclosure 1490 includes a window 1492a above the detectors 1410c, which allows light to be transmitted onto the detectors 1410c.

**[0247]** A noise shield 1403 is disposed above the shielding enclosure 1490. The noise shield 1403, in the depicted embodiment, includes a window 1492a corresponding to the window 1492a. Each of the windows 1492a, 1492b can include glass, plastic, or can be an opening without glass or plastic. In some embodiments, the windows 1492a, 1492b may be selected to have different sizes or shapes from each other.

**[0248]** The noise shield 1403 can include any of the features of the conductive glass described above. In the depicted embodiment, the noise shield 1403 extends about three-quarters of the length of the detector shell 306f. In other embodiments, the noise shield 1403 could be smaller or larger. The noise shield 1403 could, for instance, merely cover the detectors 1410c, the submount 1400c, or a portion thereof. The noise shield 1403 also includes a stop 1413 for positioning a measurement site within the sensor 301f. Advantageously, in certain embodiments, the noise shield 1403 can reduce noise caused by light piping.

**[0249]** A thermistor 1470 is also shown. The thermistor 1470 is attached to the submount 1400c and protrudes above the noise shield 1403. As described above, the thermistor 1470 can be employed to measure a temperature of a

measurement site. Such a temperature can be helpful in correcting for wavelength drift due to changes in water absorption, which can be temperature dependent, thereby providing more accurate data useful in detecting blood analytes like glucose.

**[0250]** In the depicted embodiment, the detectors 1410c are not enclosed in the cylindrical housing 1430. In an alternative embodiment, the cylindrical housing 1430 encloses the detectors 1410c and is disposed under the noise shield 1403. In another embodiment, the cylindrical housing 1430 encloses the detectors 1410c and the noise shield 1403 is not used. If both the cylindrical housing 1403 and the noise shield 1403 are used, either or both can have noise shielding features.

**[0251]** **FIGURE 14G** illustrates the detector shell 306f of **FIGURE 14F**, with the finger bed 310f disposed thereon. **FIGURE 14H** illustrates the detector shell 306f of **FIGURE 14G**, with the protrusion 605b disposed in the finger bed 310f.

**[0252]** **FIGURE 14I** illustrates a cutaway view of the sensor 301f. Not all features of the sensor 301f are shown, such as the protrusion 605b. Features shown include the emitter and detector shells 304f, 306f, the flaps 307f, the heat sink 350f and fins 351f, the finger bed 310f, and the noise shield 1403.

**[0253]** In addition to these features, emitters 1404 are depicted in the emitter shell 304f. The emitters 1404 are disposed on a submount 1401, which is connected to a circuit board 1419. The emitters 1404 are also enclosed within a cylindrical housing 1480. The cylindrical housing 1480 can include all of the features of the cylindrical housing 1430 described above. For example, the cylindrical housing 1480 can be made of metal, can be connected to a ground plane of the submount 1401 to provide noise shielding, and can include a transparent cover 1482.

**[0254]** The cylindrical housing 1480 can also protect the emitters 1404 from fluids and vapors that can cause corrosion. Moreover, the cylindrical housing 1480 can provide a gap between the emitters 1404 and the measurement site (not shown), which can allow light from the emitters 1404 to even out or average out before reaching the measurement site.

**[0255]** The heat sink 350f, in addition to including the fins 351f, includes a protuberance 352f that extends down from the fins 351f and contacts the submount 1401. The protuberance 352f can be connected to the submount 1401, for example, with thermal paste or the like. The protuberance 352f can sink heat from the emitters 1404 and dissipate the heat via the fins 351f.

**[0256]** **FIGURES 15A** and **15B** illustrate embodiments of sensor portions 1500A, 1500B that include alternative heat sink features to those described above. These features can be incorporated into any of the sensors described above. For example, any of the sensors above can be modified to use the heat sink features described below instead of or in addition to the heat sink features of the sensors described above.

**[0257]** The sensor portions 1500A, 1500B shown include LED emitters 1504; however, for ease of illustration, the detectors have been omitted. The sensor portions 1500A, 1500B shown can be included, for example, in any of the emitter shells described above.

**[0258]** The LEDs 1504 of the sensor portions 1500A, 1500B are connected to a substrate or submount 1502. The submount 1502 can be used in place of any of the submounts described above. The submount 1502 can be a non-electrically conducting material made of any of a variety of materials, such as ceramic, glass, or the like. A cable 1512 is attached to the submount 1502 and includes electrical wiring 1514, such as twisted wires and the like, for communicating with the LEDs 1504. The cable 1512 can correspond to the cables 212 described above.

**[0259]** Although not shown, the cable 1512 can also include electrical connections to a detector. Only a portion of the cable 1512 is shown for clarity. The depicted embodiment of the cable 1512 includes an outer jacket 1510 and a conductive shield 1506 disposed within the outer jacket 1510. The conductive shield 1506 can be a ground shield or the like that is made of a metal such as braided copper or aluminum. The conductive shield 1506 or a portion of the conductive shield 1506 can be electrically connected to the submount 1502 and can reduce noise in the signal generated by the sensor 1500A, 1500B by reducing RF

coupling with the wires 1514. In alternative embodiments, the cable 1512 does not have a conductive shield. For example, the cable 1512 could be a twisted pair cable or the like, with one wire of the twisted pair used as a heat sink.

**[0260]** Referring specifically to **FIGURE 15A**, in certain embodiments, the conductive shield 1506 can act as a heat sink for the LEDs 1504 by absorbing thermal energy from the LEDs 1504 and/or the submount 1502. An optional heat insulator 1520 in communication with the submount 1502 can also assist with directing heat toward the conductive shield 1506. The heat insulator 1520 can be made of plastic or another suitable material. Advantageously, using the conductive shield 1506 in the cable 1512 as a heat sink can, in certain embodiments, reduce cost for the sensor.

**[0261]** Referring to **FIGURE 15B**, the conductive shield 1506 can be attached to both the submount 1502 and to a heat sink layer 1530 sandwiched between the submount 1502 and the optional insulator 1520. Together, the heat sink layer 1530 and the conductive shield 1506 in the cable 1512 can absorb at least part of the thermal energy from the LEDs and/or the submount 1502.

**[0262]** **FIGURES 15C** and **15D** illustrate implementations of a sensor portion 1500C that includes the heat sink features of the sensor portion 1500A described above with respect to **FIGURE 15A**. The sensor portion 1500C includes the features of the sensor portion 1500A, except that the optional insulator 1520 is not shown. **FIGURE 15D** is a side cutaway view of the sensor portion 1500C that shows the emitters 1504.

**[0263]** The cable 1512 includes the outer jacket 1510 and the conductive shield 1506. The conductive shield 1506 is soldered to the submount 1502, and the solder joint 1561 is shown. In some embodiments, a larger solder joint 1561 can assist with removing heat more rapidly from the emitters 1504. Various connections 1563 between the submount 1502 and a circuit board 1519 are shown. In addition, a cylindrical housing 1580, corresponding to the cylindrical housing 1480 of **FIGURE 14I**, is shown protruding through the circuit board 1519. The emitters 1504 are enclosed in the cylindrical housing 1580.

**[0264]** **FIGURES 15E** and **15F** illustrate implementations of a sensor portion 1500E that includes the heat sink features of the sensor portion 1500B described above with respect to **FIGURE 15B**. The sensor portion 1500E includes the heat sink layer 1530. The heat sink layer 1530 can be a metal plate, such as a copper plate or the like. The optional insulator 1520 is not shown. **FIGURE 15F** is a side cutaway view of the sensor portion 1500E that shows the emitters 1504.

**[0265]** In the depicted embodiment, the conductive shield 1506 of the cable 1512 is soldered to the heat sink layer 1530 instead of the submount 1502. The solder joint 1565 is shown. In some embodiments, a larger solder joint 1565 can assist with removing heat more rapidly from the emitters 1504. Various connections 1563 between the submount 1502 and a circuit board 1519 are shown. In addition, the cylindrical housing 1580 is shown protruding through the circuit board 1519. The emitters 1504 are enclosed in the cylindrical housing 1580.

**[0266]** **FIGURES 15G** and **15H** illustrate embodiments of connector features that can be used with any of the sensors described above with respect to **FIGURES 1** through **15F**. Referring to **FIGURE 15G**, the circuit board 1519 includes a female connector 1575 that mates with a male connector 1577 connected to a daughter board 1587. The daughter board 1587 includes connections to the electrical wiring 1514 of the cable 1512. The connected boards 1519, 1587 are shown in **FIGURE 15H**. Also shown is a hole 1573 that can receive the cylindrical housing 1580 described above.

**[0267]** Advantageously, in certain embodiments, using a daughter board 1587 to connect to the circuit board 1519 can enable connections to be made more easily to the circuit board 1519. In addition, using separate boards can be easier to manufacture than a single circuit board 1519 with all connections soldered to the circuit board 1519.

**[0268]** **FIGURE 15I** illustrates an exemplary architecture for front-end interface 108 as a transimpedance-based front-end. As noted, front-end interfaces 108 provide an interface that adapts the output of detectors 106 into a form that can be handled by signal processor 110. As shown in this figure, sensor 101 and front-end interfaces 108 may be integrated together as a single component, such as an

integrated circuit. Of course, one skilled in the art will recognize that sensor 101 and front end interfaces 108 may comprise multiple components or circuits that are coupled together.

**[0269]** Front-end interfaces 108 may be implemented using transimpedance amplifiers that are coupled to analog to digital converters in a sigma delta converter. In some embodiments, a programmable gain amplifier (PGA) can be used in combination with the transimpedance-based front-ends. For example, the output of a transimpedance-based front-end may be output to a sigma-delta ADC that comprises a PGA. A PGA may be useful in order to provide another level of amplification and control of the stream of signals from detectors 106. The PGA may be an integrated circuit or built from a set of micro-relays. Alternatively, the PGA and ADC components in converter 900 may be integrated with the transimpedance-based front-end in sensor 101.

**[0270]** Due to the low-noise requirements for measuring blood analytes like glucose and the challenge of using multiple photodiodes in detector 106, the applicants developed a noise model to assist in configuring front-end 108. Conventionally, those skilled in the art have focused on optimizing the impedance of the transimpedance amplifiers to minimize noise.

**[0271]** However, the following noise model was discovered by the applicants:

$$Noise = \sqrt{aR + bR^2}, \text{ where:}$$

**[0272]**  $aR$  is characteristic of the impedance of the transimpedance amplifier; and

**[0273]**  $bR^2$  is characteristic of the impedance of the photodiodes in detector and the number of photodiodes in detector 106.

**[0274]** The foregoing noise model was found to be helpful at least in part due to the high SNR required to measure analytes like glucose. However, the foregoing noise model was not previously recognized by artisans at least in part because, in conventional devices, the major contributor to noise was generally believed to originate from the emitter or the LEDs. Therefore, artisans have generally continued to focus on reducing noise at the emitter.

[0275] However, for analytes like glucose, the discovered noise model revealed that one of the major contributors to noise was generated by the photodiodes. In addition, the amount of noise varied based on the number of photodiodes coupled to a transimpedance amplifier. Accordingly, combinations of various photodiodes from different manufacturers, different impedance values with the transimpedance amplifiers, and different numbers of photodiodes were tested as possible embodiments.

[0276] In some embodiments, different combinations of transimpedance to photodiodes may be used. For example, detectors 1-4 (as shown, e.g., in **FIGURE 12A**) may each comprise four photodiodes. In some embodiments, each detector of four photodiodes may be coupled to one or more transimpedance amplifiers. The configuration of these amplifiers may be set according to the model shown in **FIGURE 15J**.

[0277] Alternatively, each of the photodiodes may be coupled to its own respective transimpedance amplifier. For example, transimpedance amplifiers may be implemented as integrated circuits on the same circuit board as detectors 1-4. In this embodiment, the transimpedance amplifiers may be grouped into an averaging (or summing) circuit, which are known to those skilled in the art, in order to provide an output stream from the detector. The use of a summing amplifier to combine outputs from several transimpedance amplifiers into a single, analog signal may be helpful in improving the SNR relative to what is obtainable from a single transimpedance amplifier. The configuration of the transimpedance amplifiers in this setting may also be set according to the model shown in **FIGURE 15J**.

[0278] As yet another alternative, as noted above with respect to **FIGURES 12E** through **12H**, the photodiodes in detectors 106 may comprise multiple active areas that are grouped together. In some embodiments, each of these active areas may be provided its own respective transimpedance. This form of pairing may allow a transimpedance amplifier to be better matched to the characteristics of its corresponding photodiode or active area of a photodiode.

[0279] As noted, **FIGURE 15J** illustrates an exemplary noise model that may be useful in configuring transimpedance amplifiers. As shown, for a given



number of photodiodes and a desired SNR, an optimal impedance value for a transimpedance amplifier could be determined.

**[0280]** For example, an exemplary “4 PD per stream” sensor 1502 is shown where detector 106 comprises four photodiodes 1502. The photodiodes 1502 are coupled to a single transimpedance amplifier 1504 to produce an output stream 1506. In this example, the transimpedance amplifier comprises 10 M $\Omega$  resistors 1508 and 1510. Thus, output stream 1506 is produced from the four photodiodes (PD) 1502. As shown in the graph of **FIGURE 15J**, the model indicates that resistance values of about 10 M $\Omega$  may provide an acceptable SNR for analytes like glucose.

**[0281]** However, as a comparison, an exemplary “1 PD per stream” sensor 1512 is also shown in **FIGURE 15J**. In particular, sensor 1512 may comprise a plurality of detectors 106 that each comprises a single photodiode 1514. In addition, as shown for this example configuration, each of photodiodes 1514 may be coupled to respective transimpedance amplifiers 1516, e.g., 1 PD per stream. Transimpedance amplifiers are shown having 40 M $\Omega$  resistors 1518. As also shown in the graph of **FIGURE 15J**, the model illustrates that resistance values of 40 M $\Omega$  for resistors 1518 may serve as an alternative to the 4 photodiode per stream architecture of sensor 1502 described above and yet still provide an equivalent SNR.

**[0282]** Moreover, the discovered noise model also indicates that utilizing a 1 photodiode per stream architecture like that in sensor 1512 may provide enhanced performance because each of transimpedance amplifiers 1516 can be tuned or optimized to its respective photodiodes 1518. In some embodiments, an averaging component 1520 may also be used to help cancel or reduce noise across photodiodes 1518.

**[0283]** For purposes of illustration, **FIGURE 15K** shows different architectures (e.g., four PD per stream and one PD per stream) for various embodiments of a sensor and how components of the sensor may be laid out on a circuit board or substrate. For example, sensor 1522 may comprise a “4 PD per stream” architecture on a submount 700 in which each detector 106 comprises four

(4) photodiodes 1524. As shown for sensor 1522, the output of each set of four photodiodes 1524 is then aggregated into a single transimpedance amplifier 1526 to produce a signal.

**[0284]** As another example, a sensor 1528 may comprise a “1 PD per stream” architecture on submount 700 in which each detector 106 comprises four (4) photodiodes 1530. In sensor 1528, each individual photodiode 1530 is coupled to a respective transimpedance amplifier 1532. The output of the amplifiers 1532 may then be aggregated into averaging circuit 1520 to produce a signal.

**[0285]** As noted previously, one skilled in the art will recognize that the photodiodes and detectors may be arranged in different fashions to optimize the detected light. For example, sensor 1534 illustrates an exemplary “4 PD per stream” sensor in which the detectors 106 comprise photodiodes 1536 arranged in a linear fashion. Likewise, sensor 1538 illustrates an exemplary “1 PD per stream” sensor in which the detectors comprise photodiodes 1540 arranged in a linear fashion.

**[0286]** Alternatively, sensor 1542 illustrates an exemplary “4 PD per stream” sensor in which the detectors 106 comprise photodiodes 1544 arranged in a two-dimensional pattern, such as a zig-zag pattern. Sensor 1546 illustrates an exemplary “1 PD per stream” sensor in which the detectors comprise photodiodes 1548 also arranged in a zig-zag pattern.

**[0287]** **FIGURE 15L** illustrates an exemplary architecture for a switched-capacitor-based front-end. As shown, front-end interfaces 108 may be implemented using switched capacitor circuits and any number of front-end interfaces 108 may be implemented. The output of these switched capacitor circuits may then be provided to a digital interface 1000 and signal processor 110. Switched capacitor circuits may be useful in system 100 for their resistor free design and analog averaging properties. In particular, the switched capacitor circuitry provides for analog averaging of the signal that allows for a lower smaller sampling rate (e.g., 2 KHz sampling for analog versus 48 KHz sampling for digital designs) than similar digital designs. In some embodiments, the switched capacitor architecture in front end interfaces 108 may provide a similar or equivalent SNR to other front end designs,

such as a sigma delta architecture. In addition, a switched capacitor design in front end interfaces 108 may require less computational power by signal processor 110 to perform the same amount of decimation to obtain the same SNR.

**[0288] FIGURES 16A and 16B** illustrate embodiments of disposable optical sensors 1600. In an embodiment, any of the features described above, such as protrusion, shielding, and/or heat sink features, can be incorporated into the disposable sensors 1600 shown. For instance, the sensors 1600 can be used as the sensors 101 in the system 100 described above with respect to FIGURE 1. Moreover, any of the features described above, such as protrusion, shielding, and/or heat sink features, can be implemented in other disposable sensor designs that are not depicted herein.

**[0289]** The sensors 1600 include an adult/pediatric sensor 1610 for finger placement and a disposable infant/neonate sensor 1602 configured for toe, foot or hand placement. Each sensor 1600 has a tape end 1610 and an opposite connector end 1620 electrically and mechanically interconnected via a flexible coupling 1630. The tape end 1610 attaches an emitter and detector to a tissue site. Although not shown, the tape end 1610 can also include any of the protrusion, shielding, and/or heat sink features described above. The emitter illuminates the tissue site and the detector generates a sensor signal responsive to the light after tissue absorption, such as absorption by pulsatile arterial blood flow within the tissue site.

**[0290]** The sensor signal is communicated via the flexible coupling 1630 to the connector end 1620. The connector end 1620 can mate with a cable (not shown) that communicates the sensor signal to a monitor (not shown), such as any of the cables or monitors shown above with respect to FIGURES 2A through 2D. Alternatively, the connector end 1620 can mate directly with the monitor.

**[0291] FIGURE 17** illustrates an exploded view of certain of the components of the sensor 301f described above. A heat sink 1751 and a cable 1781 attach to an emitter shell 1704. The emitter shell attaches to a flap housing 1707. The flap housing 1707 includes a receptacle 1709 to receive a cylindrical

housing 1480/1580 (not shown) attached to an emitter submount 1702, which is attached to a circuit board 1719.

**[0292]** A spring 1787 attaches to a detector shell 1706 via pins 1783, 1785, which hold the emitter and detector shells 1704, 1706 together. A support structure 1791 attaches to the detector shell 1706, which provides support for a shielding enclosure 1790. A noise shield 1713 attaches to the shielding enclosure 1790. A detector submount 1700 is disposed inside the shielding enclosure 1790. A finger bed 1710 provides a surface for placement of the patient's finger. Finger bed 1710 may comprise a gripping surface or gripping features, which may assist in placing and stabilizing a patient's finger in the sensor. A partially cylindrical protrusion 1705 may also be disposed in the finger bed 1710. As shown, finger bed 1710 attaches to the noise shield 1703. The noise shield 1703 may be configured to reduce noise, such as from ambient light and electromagnetic noise. For example, the noise shield 1703 may be constructed from materials having an opaque color, such as black or a dark blue, to prevent light piping.

**[0293]** Noise shield 1703 may also comprise a thermistor 1712. The thermistor 1712 may be helpful in measuring the temperature of a patient's finger. For example, the thermistor 1712 may be useful in detecting when the patient's finger is reaching an unsafe temperature that is too hot or too cold. In addition, the temperature of the patient's finger may be useful in indicating to the sensor the presence of low perfusion as the temperature drops. In addition, the thermistor 1712 may be useful in detecting a shift in the characteristics of the water spectrum in the patient's finger, which can be temperature dependent.

**[0294]** Moreover, a flex circuit cover 1706 attaches to the pins 1783, 1785. Although not shown, a flex circuit can also be provided that connects the circuit board 1719 with the submount 1700 (or a circuit board to which the submount 1700 is connected). A flex circuit protector 1760 may be provided to provide a barrier or shield to the flex circuit (not shown). In particular, the flex circuit protector 1760 may also prevent any electrostatic discharge to or from the flex circuit. The flex circuit protector 1760 may be constructed from well known materials, such as a plastic or rubber materials.

**[0295]** **FIGURE 18** shows the results obtained by an exemplary sensor 101 of the present disclosure that was configured for measuring glucose. This sensor 101 was tested using a pure water ex-vivo sample. In particular, ten samples were prepared that ranged from 0-55 mg/dL. Two samples were used as a training set and eight samples were then used as a test population. As shown, embodiments of the sensor 101 were able to obtain at least a standard deviation of 13 mg/dL in the training set and 11 mg/dL in the test population.

**[0296]** **FIGURE 19** shows the results obtained by an exemplary sensor 101 of the present disclosure that was configured for measuring glucose. This sensor 101 was tested using a turbid ex-vivo sample. In particular, 25 samples of water/glucose/Lyposin were prepared that ranged from 0-55 mg/dL. Five samples were used as a training set and 20 samples were then used as a test population. As shown, embodiments of sensor 101 were able to obtain at least a standard deviation of 37 mg/dL in the training set and 32 mg/dL in the test population.

**[0297]** **FIGURES 20 through 22** shows other results that can be obtained by an embodiment of system 100. In **FIGURE 20**, 150 blood samples from two diabetic adult volunteers were collected over a 10-day period. Invasive measurements were taken with a YSI glucometer to serve as a reference measurement. Noninvasive measurements were then taken with an embodiment of system 100 that comprised four LEDs and four independent detector streams. As shown, the system 100 obtained a correlation of about 85% and Arms of about 31 mg/dL.

**[0298]** In **FIGURE 21**, 34 blood samples were taken from a diabetic adult volunteer collected over a 2-day period. Invasive measurements were also taken with a glucometer for comparison. Noninvasive measurements were then taken with an embodiment of system 100 that comprised four LEDs in emitter 104 and four independent detector streams from detectors 106. As shown, the system 100 was able to attain a correlation of about 90% and Arms of about 22 mg/dL.

**[0299]** The results shown in **FIGURE 22** relate to total hemoglobin testing with an exemplary sensor 101 of the present disclosure. In particular, 47 blood samples were collected from nine adult volunteers. Invasive measurements were

then taken with a CO-oximeter for comparison. Noninvasive measurements were taken with an embodiment of system 100 that comprised four LEDs in emitter 104 and four independent detector channels from detectors 106. Measurements were averaged over 1 minute. As shown, the testing resulted in a correlation of about 93% and Arms of about 0.8 mg/dL.

**[0300]** Conditional language used herein, such as, among others, "can," "could," "might," "may," "e.g.," and the like, unless specifically stated otherwise, or otherwise understood within the context as used, is generally intended to convey that certain embodiments include, while other embodiments do not include, certain features, elements and/or states. Thus, such conditional language is not generally intended to imply that features, elements and/or states are in any way required for one or more embodiments or that one or more embodiments necessarily include logic for deciding, with or without author input or prompting, whether these features, elements and/or states are included or are to be performed in any particular embodiment.

**[0301]** While certain embodiments of the inventions disclosed herein have been described, these embodiments have been presented by way of example only, and are not intended to limit the scope of the inventions disclosed herein. Indeed, the novel methods and systems described herein can be embodied in a variety of other forms; furthermore, various omissions, substitutions and changes in the form of the methods and systems described herein can be made without departing from the spirit of the inventions disclosed herein. The claims and their equivalents are intended to cover such forms or modifications as would fall within the scope and spirit of certain of the inventions disclosed herein.

WHAT IS CLAIMED IS:

1. A noninvasive device capable of producing a signal responsive to light attenuated by tissue at a measurement site, the device comprising:

an optical source configured to emit optical radiation at least at wavelengths between about 1600 nm and about 1700 nm; and

a plurality of photodetectors each configured to detect the optical radiation from said optical source after attenuation by said tissue of said measurement site and each output a respective signal stream responsive to said detected optical radiation.

2. The device of claim 1, wherein the optical source is configured to emit optical radiation at wavelengths from about 1600 to about 1670 nm.

3. The device of claim 1, wherein the optical source is configured to emit three wavelengths of optical radiation between about 1600 to about 1700 nm.

4. The device of claim 3, wherein the optical source is configured to emit optical radiation at three wavelengths about 30 nm apart.

5. The device of claim 3, wherein the optical source is configured to emit optical radiation at about 1610 nm, about 1645 nm, and about 1665 nm.

6. The device of claim 1, comprising a patient monitor capable of processing the plurality of output signal streams to determine output values for one or more physiological parameters.

7. The device of claim 6, wherein one of the one or more physiological parameters comprises glucose.

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8. A noninvasive, physiological sensor capable of outputting a signal responsive to a blood analyte present in a monitored patient, said sensor comprising:

a sensor housing;

an optical source positioned by said housing with respect to a tissue site of a patient when said housing is applied to the patient; and

photodetectors positioned by said housing with respect to said tissue site when said housing is applied to the patient with a variation in path length among at least some of the photodetectors from the optical source, the photodetectors configured to detect a sequence of optical radiation from said optical source after attenuation by tissue of said tissue site, said photodetectors each configured to output a respective signal stream responsive to said detected sequence of optical radiation and wherein an output signal responsive to one or more of the signal streams is usable to determine the blood analyte based at least in part on the variation in path length.

9. The sensor of claim 8, wherein the blood analyte comprises glucose, wherein the sensor comprises electronic circuitry configured to receive said signals responsive to said detected sequence of optical radiation and wherein said output signal is indicative of said glucose.

10. The sensor of claim 8, comprising a display coupled to the sensor housing and configured to display information indicating the blood analyte.

11. The sensor of claim 6, comprising a signal medium that is configured to connect to a processing device.

12. The sensor of claim 8, further comprising an interface configured to provide the signal to a device external to the sensor.

13. The sensor of claim 12, wherein the interface comprises at least one transimpedance amplifier configured to amplify the signal stream from the photodetectors.



14. The sensor of claim 12, wherein the interface comprises at least one switched capacitor circuit configured to convert said signal stream from the photodetectors into digital information.

15. The sensor of claim 8, wherein the housing comprises a shell constructed of material capable of reflecting at least some of the optical radiation back into the tissue site.

16. The sensor of claim 6, wherein the optical source comprises at least one set of sources comprising at least one light emitting diode and at least one super-luminescent light emitting diode.

17. The sensor of claim 16, wherein the light emitting diode is configured to transmit optical radiation at a wavelength of approximately 900 to approximately 1300 nm.

18. The sensor of claim 16, wherein the super-luminescent light emitting diode is configured to transmit optical radiation at a wavelength of approximately 1650 to approximately 1800 nm.

19. The sensor of claim 8, wherein the photodetectors are housed within optically separate compartments that reduce mixing of optical radiation from different regions of the tissue site.

20. The sensor of claim 8, further comprising an optical noise reducer capable of reducing ambient light from entering the tissue site.

21. The sensor of claim 8, further comprising a heat sink configured to dissipate heat from the sensor.

22. The sensor of claim 8, wherein the photodetectors are arranged in a special geometry.

23. The sensor of claim 22, wherein the special geometry comprises a substantially linear geometry.

24. The sensor of claim 23, wherein the special substantially linear geometry comprises substantially equal spacing.

25. The sensor of claim 23, wherein the special substantially linear geometry comprises substantially unequal spacing.

26. The sensor of claim 23, wherein the special substantially linear geometry comprises substantially logarithmic spacing.

27. The sensor of claim 23, wherein the special substantially linear geometry comprises substantially progressive spacing.

28. The sensor of claim 22, wherein the special geometry comprises a substantially grid geometry.

29. A method of measuring an analyte based on multiple streams of optical radiation measured from a measurement site, said method comprising:

emitting a sequence of optical radiation pulses to the measurement site;

detecting at a first location a first stream of optical radiation from the measurement site;

detecting at least at one additional location different from the first location an additional stream of optical radiation from the measurement site;  
and

determining an output measurement value indicative of the analyte based on the detected streams of optical radiation.

30. The method of claim 29, wherein said analyte comprises glucose.

31. The method of claim 29, further comprising converting the detected streams of optical radiation into a digital signal including a respective stream for each location.

32. The method of claim 29, wherein said emitting comprises emitting light from at least one light emitting diode and at least one super-luminescent light emitting diode.

33. The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 900 to approximately 1300 nm.

34. The method of claim 29, wherein said emitting comprises emitting at least one pulse at a wavelength of approximately 1650 to approximately 1800 nm.

**MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE  
MEASUREMENT OF BLOOD CONSTITUENTS  
ABSTRACT OF THE DISCLOSURE**

The present disclosure relates to noninvasive methods, devices, and systems for measuring various blood constituents or analytes, such as glucose. In an embodiment, a light source comprises LEDs and super-luminescent LEDs. The light source emits light at least wavelengths of about 1610 nm, about 1640 nm, and about 1665 nm. In an embodiment, the detector comprises a plurality of photodetectors arranged in a special geometry comprising one of a substantially linear substantially equal spaced geometry, a substantially linear substantially non-equal spaced geometry, and a substantially grid geometry.

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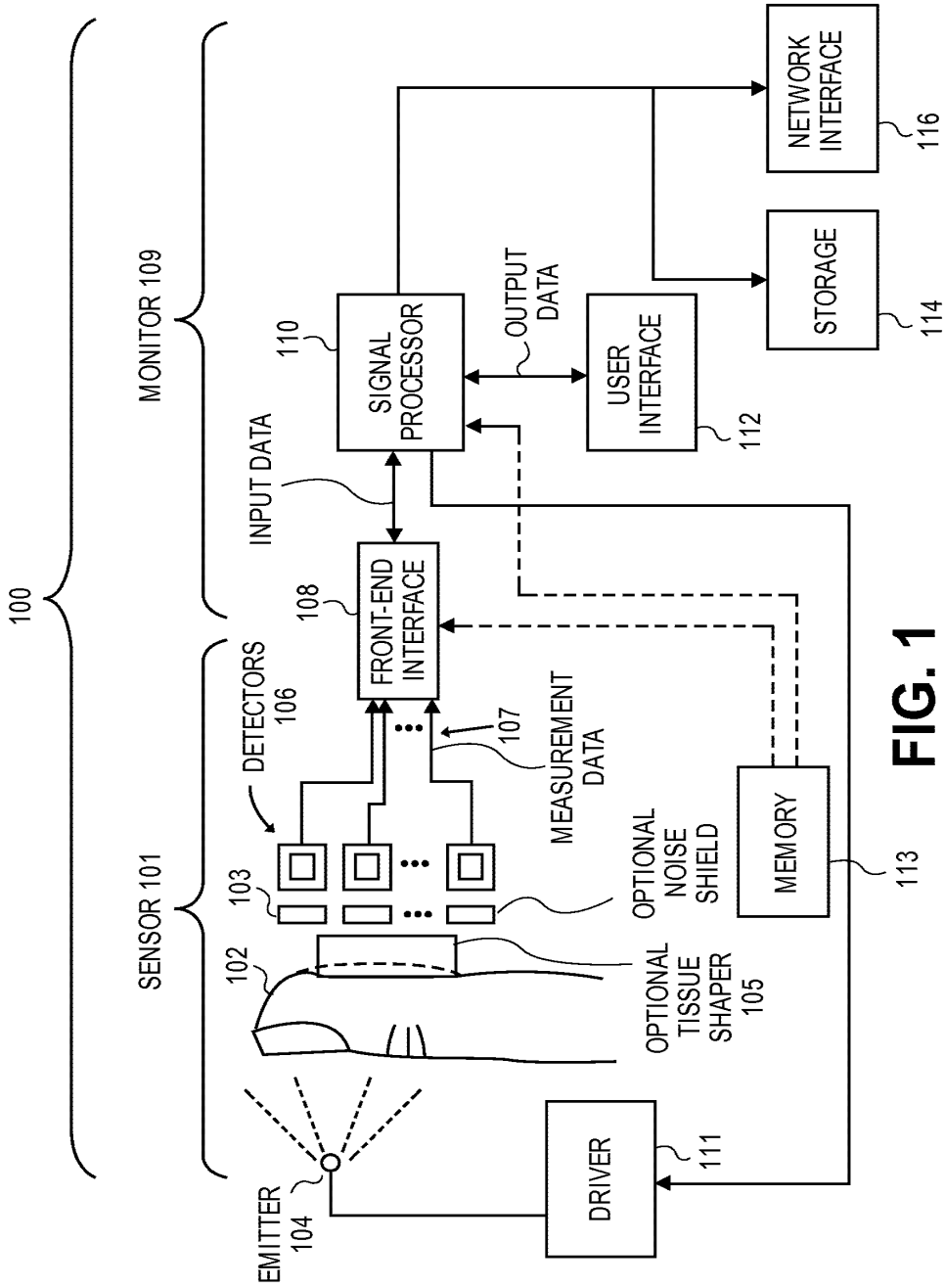
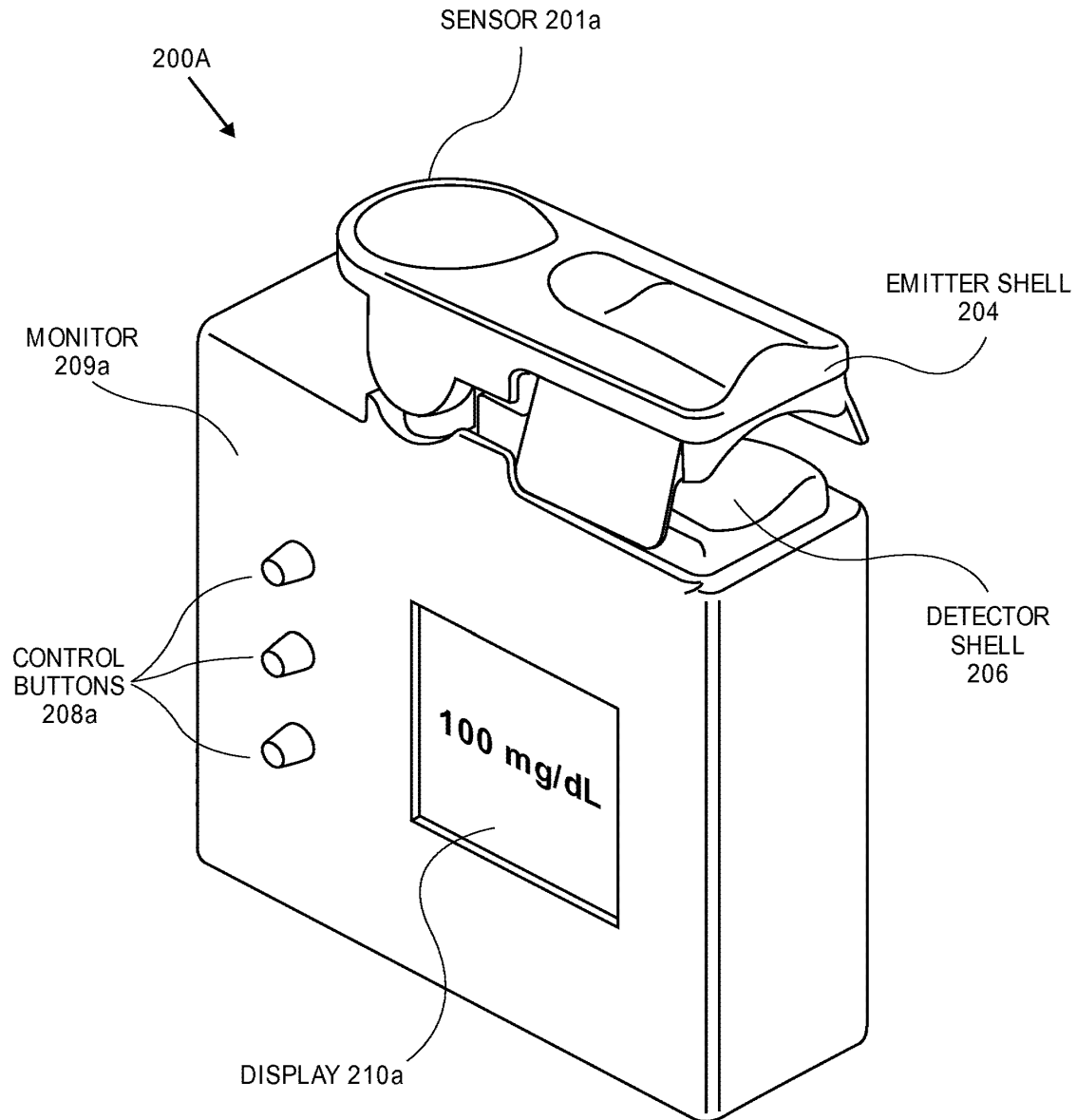


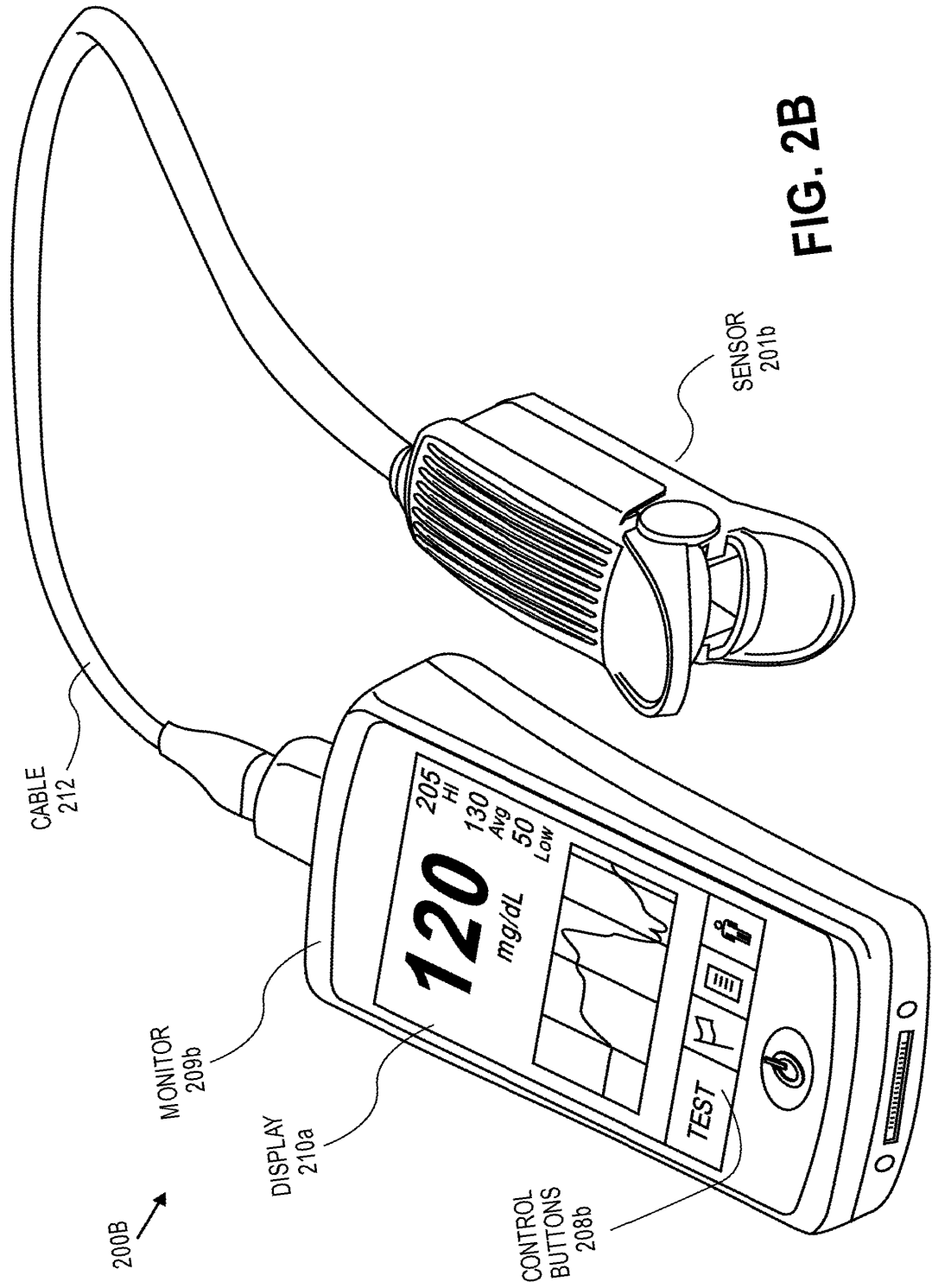
FIG. 1

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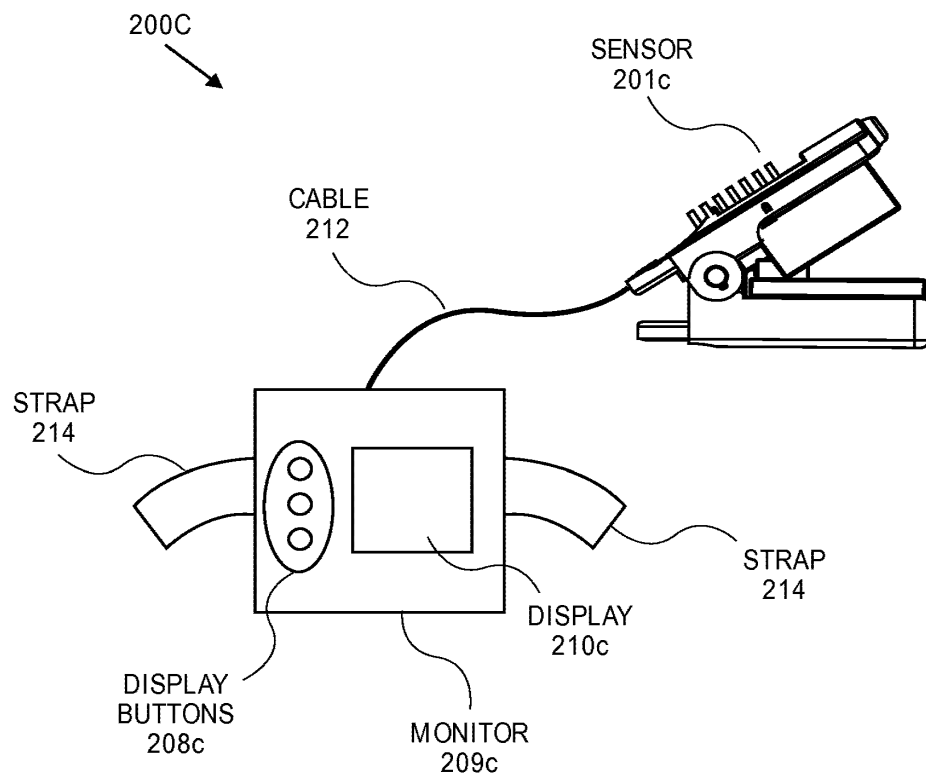
**FIG. 2A**

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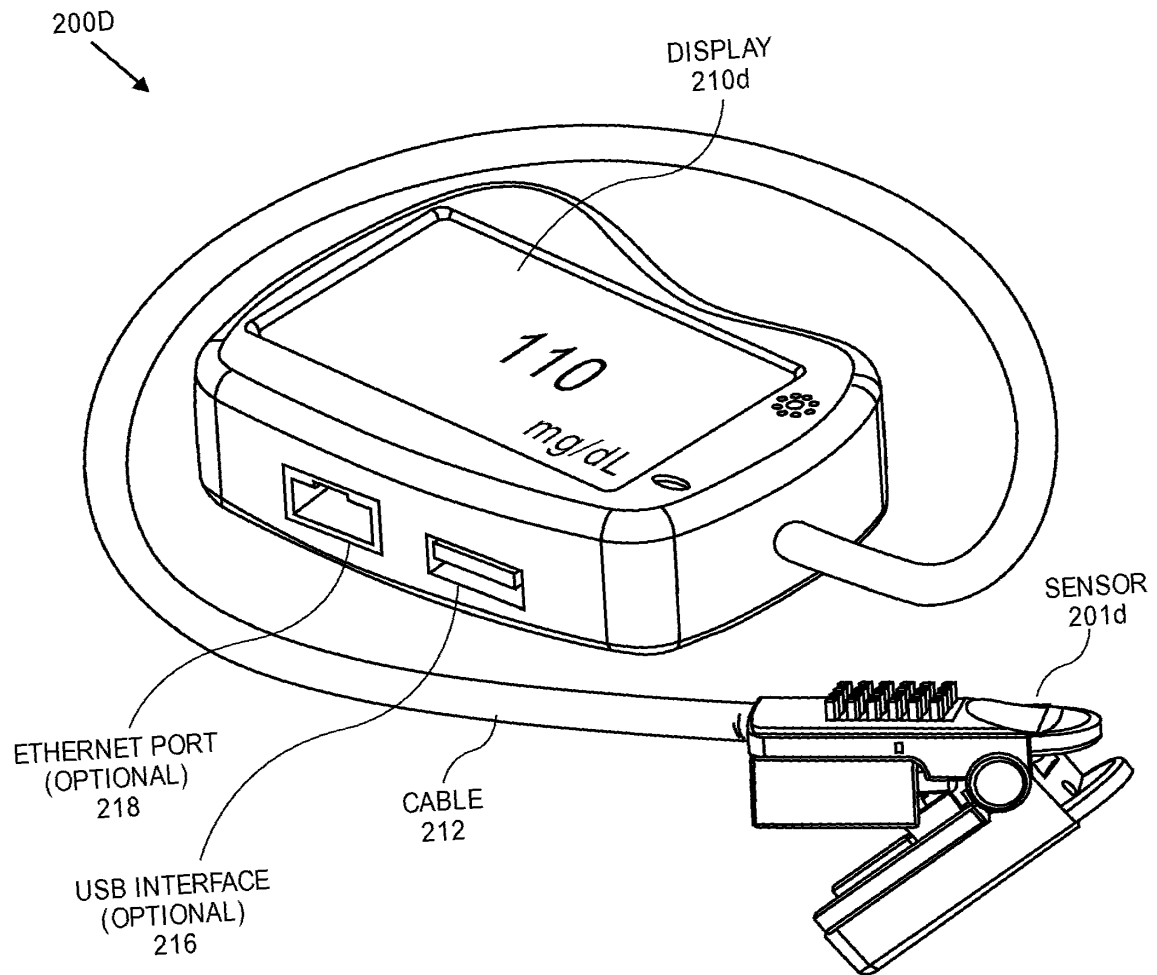
**FIG. 2B**

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**FIG. 2C**

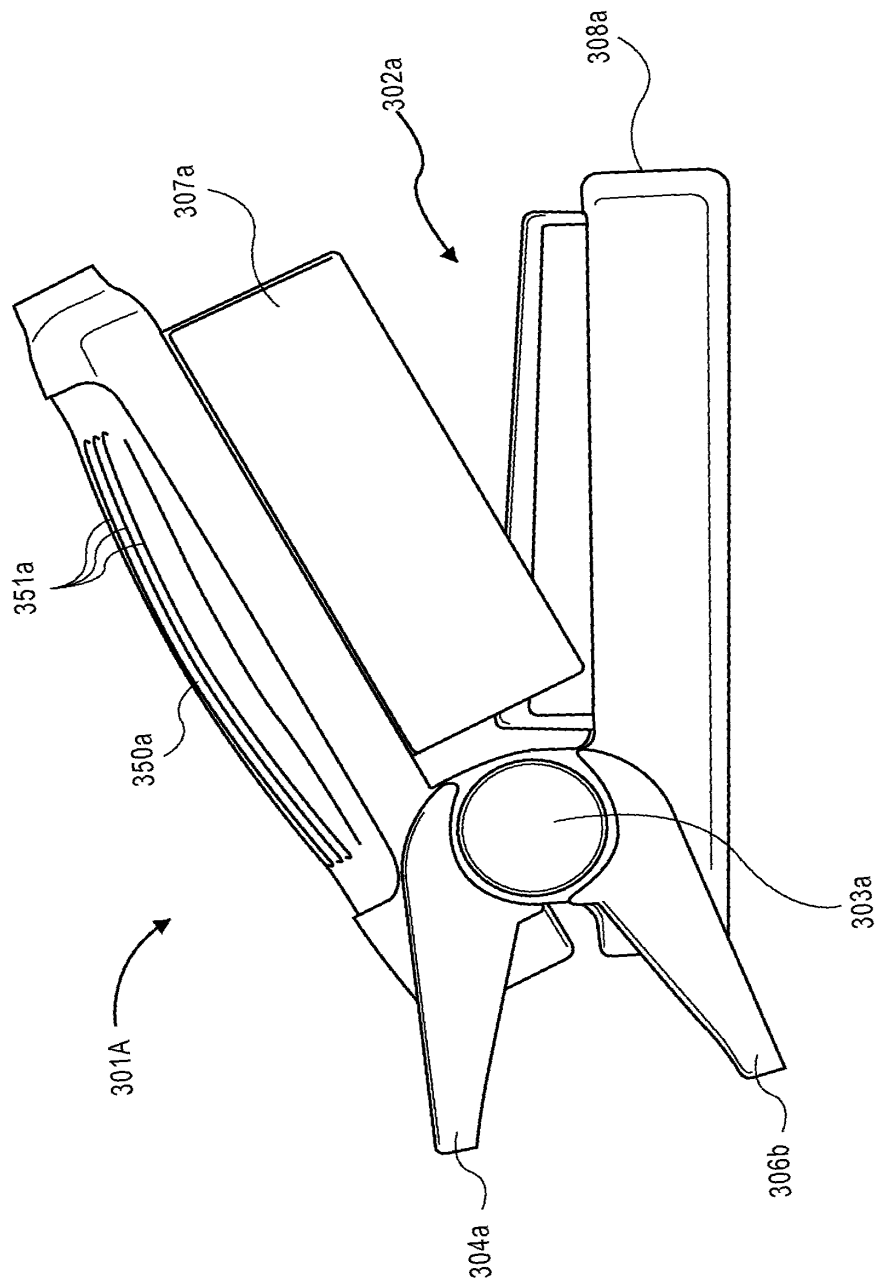
5/65



**FIG. 2D**

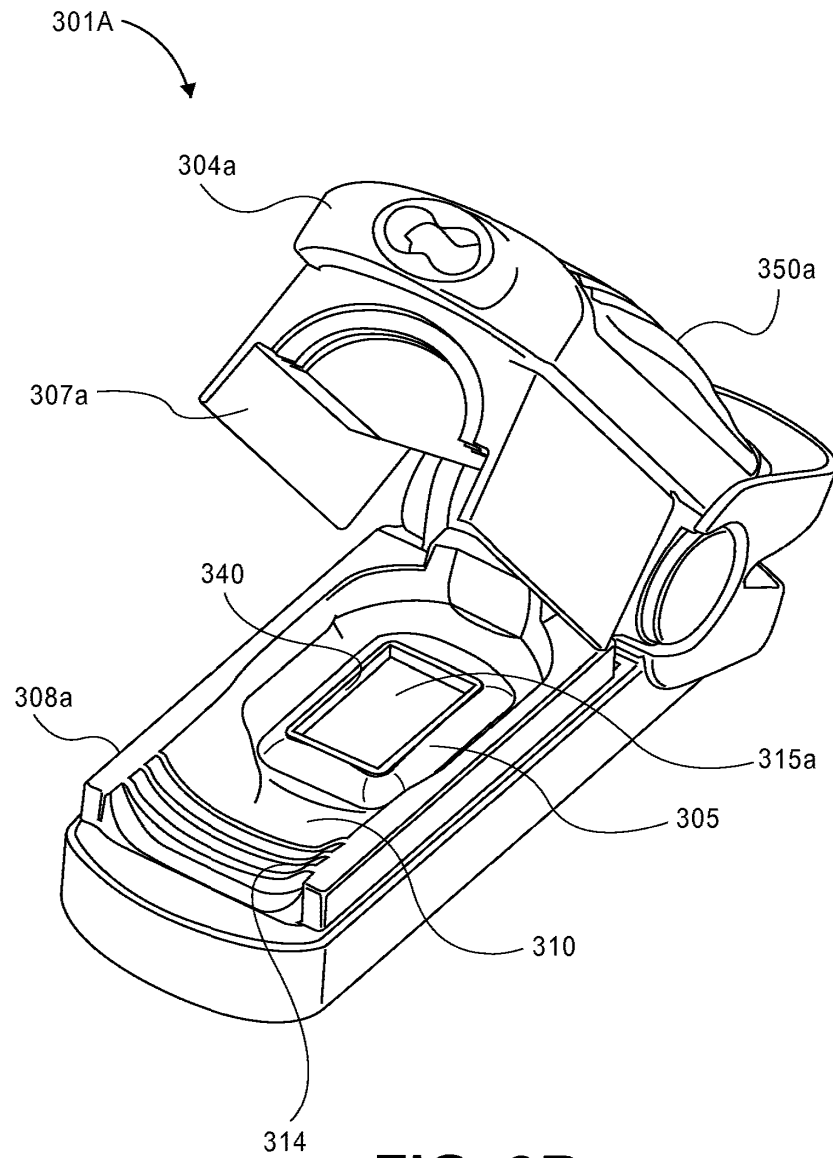


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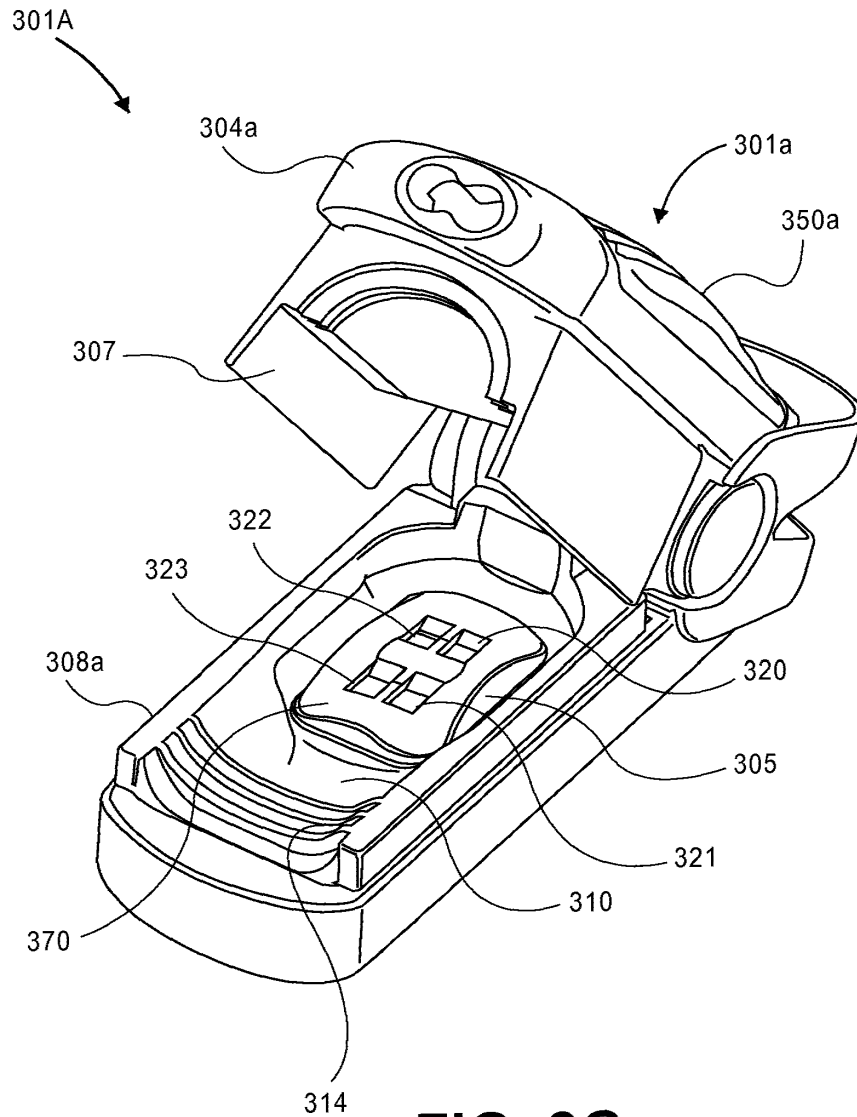
**FIG. 3A**

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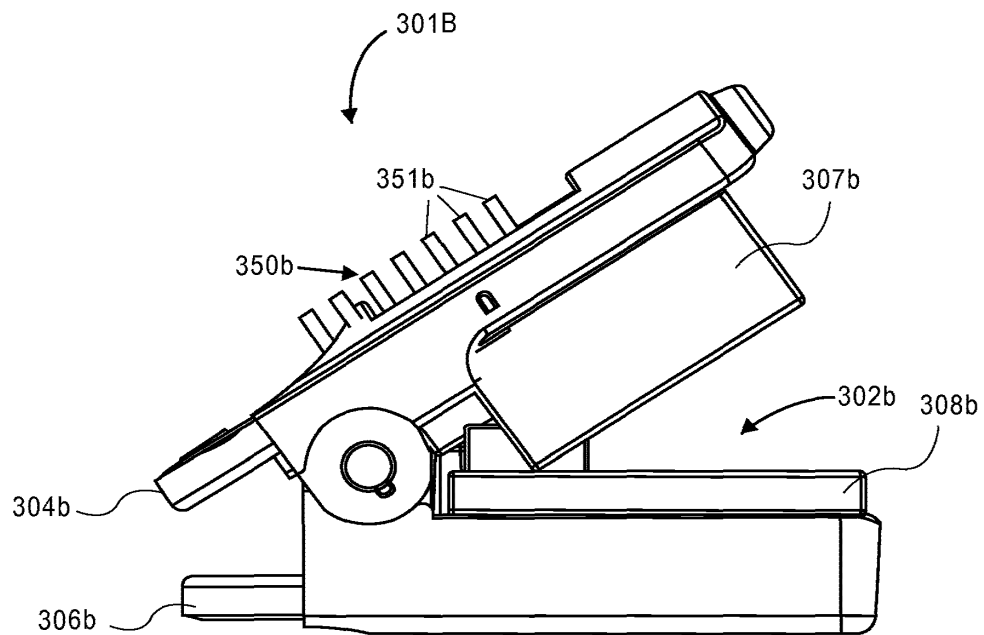
**FIG. 3B**

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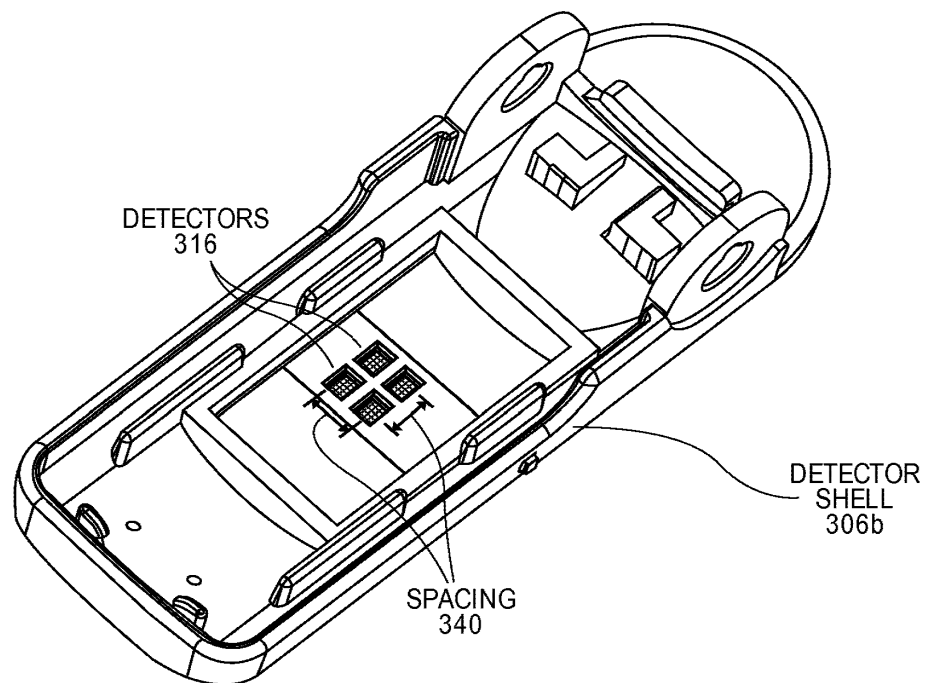
**FIG. 3C**

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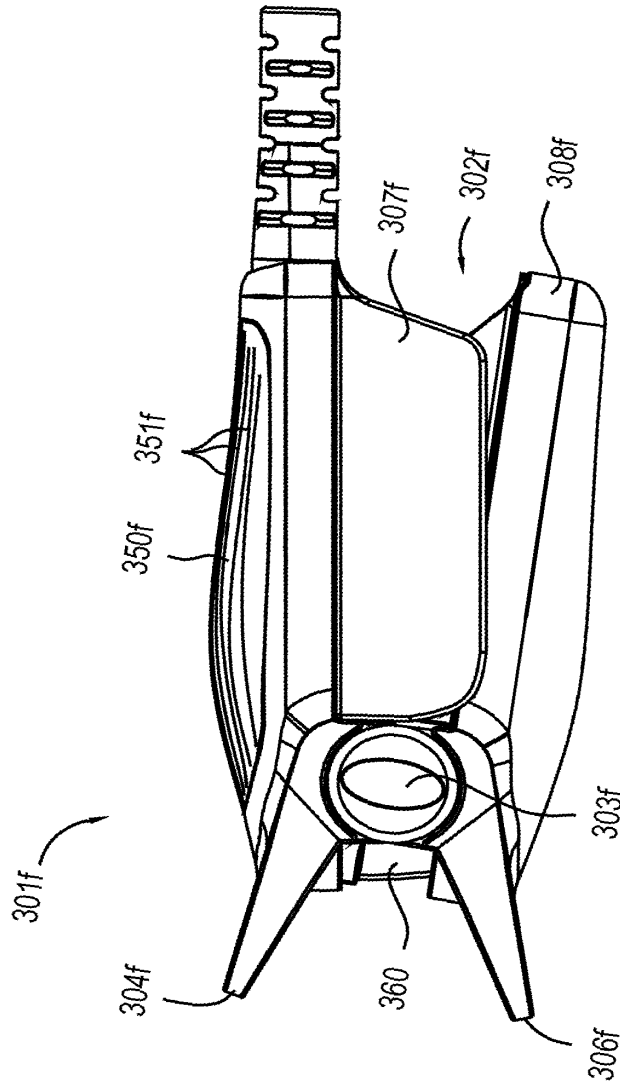


**FIG. 3D**

10/65



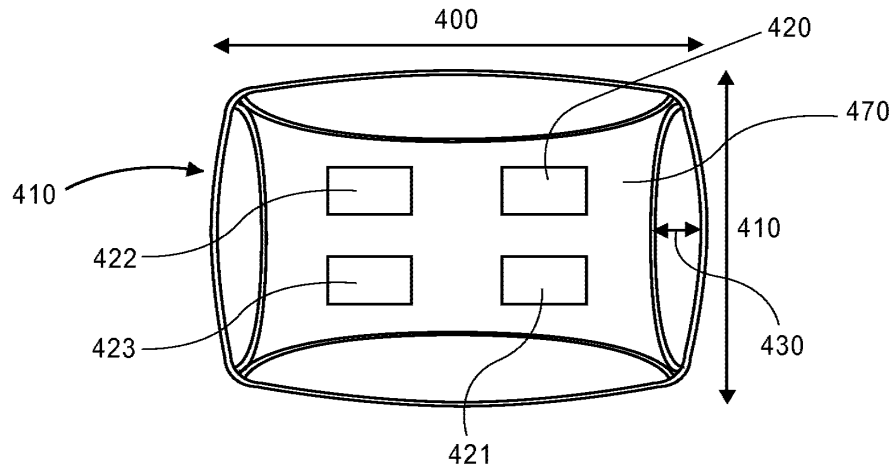
**FIG. 3E**



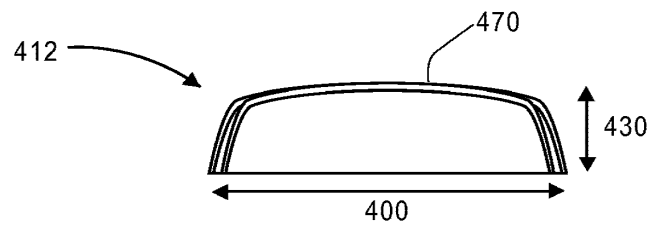
**FIG. 3F**

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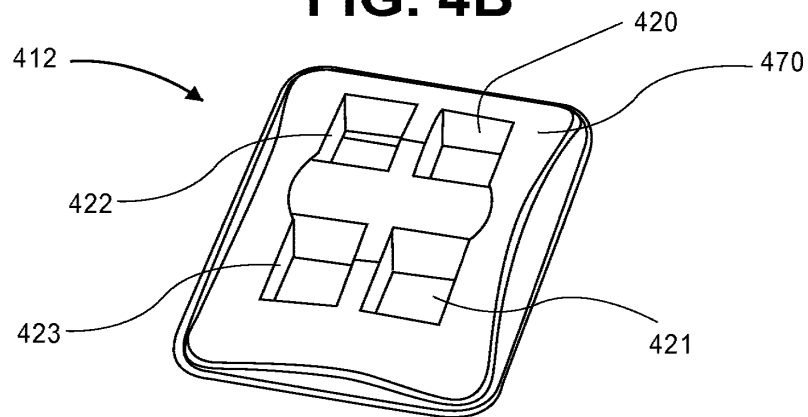
12/65



**FIG. 4A**



**FIG. 4B**



**FIG. 4C**

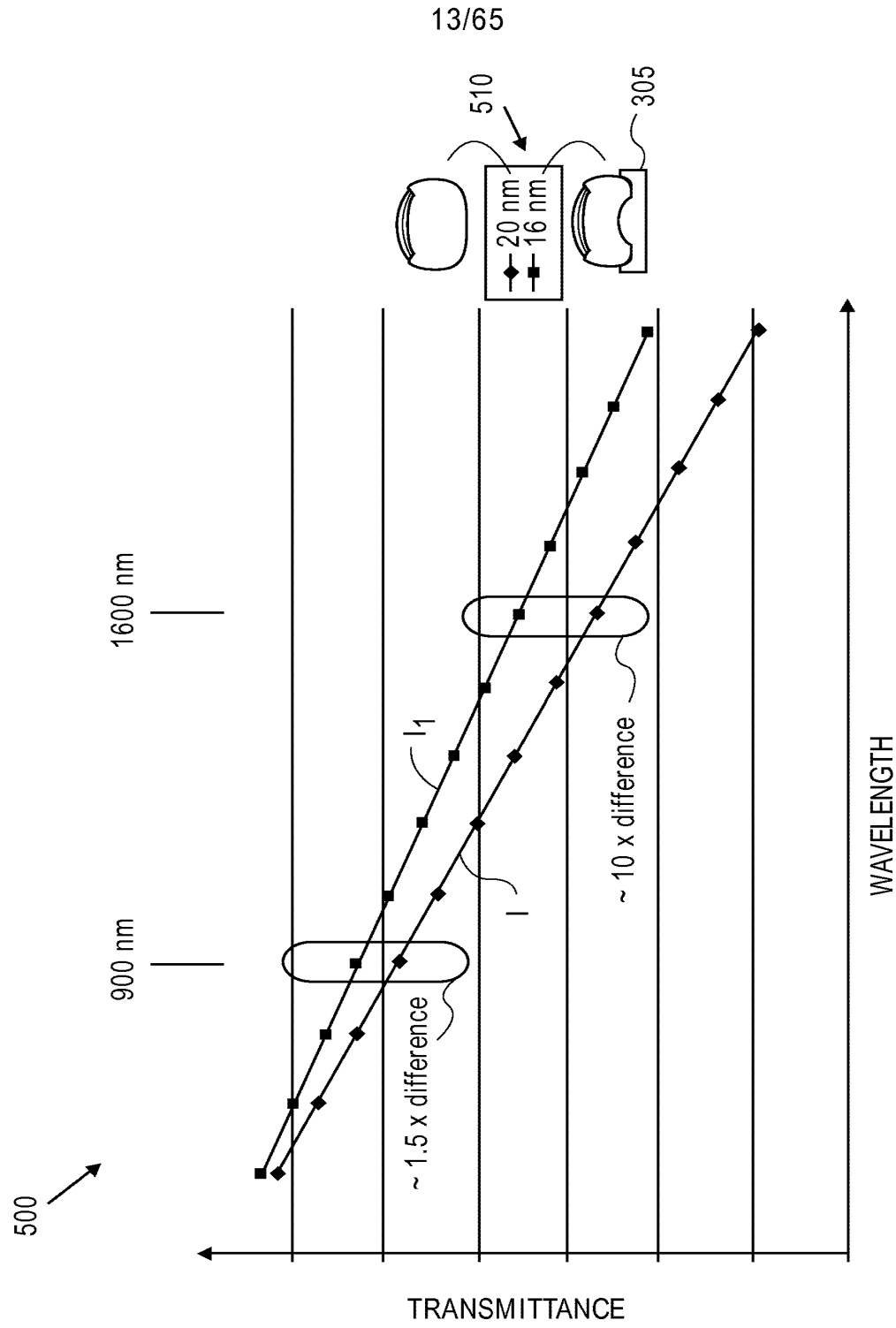
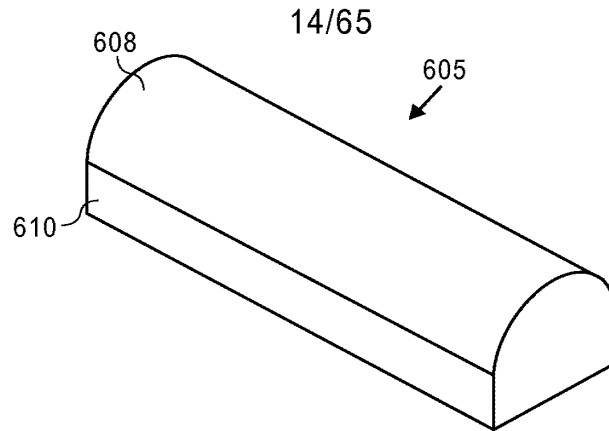
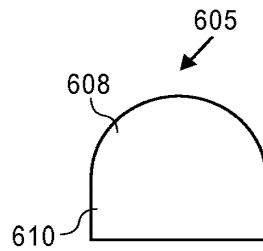


FIG. 5

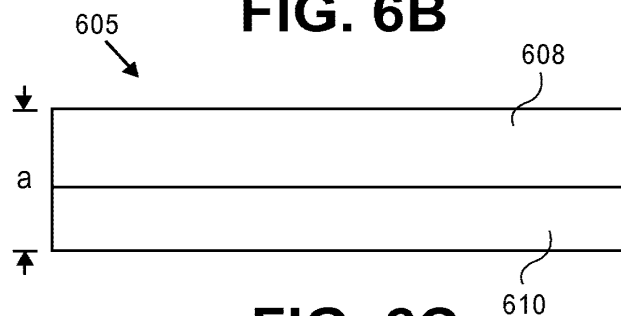




**FIG. 6A**



**FIG. 6B**



**FIG. 6C**



**FIG. 6D**

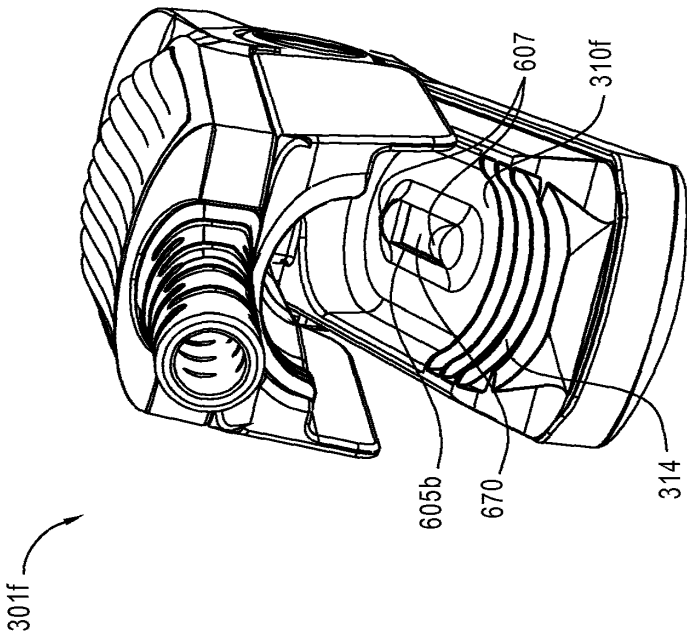
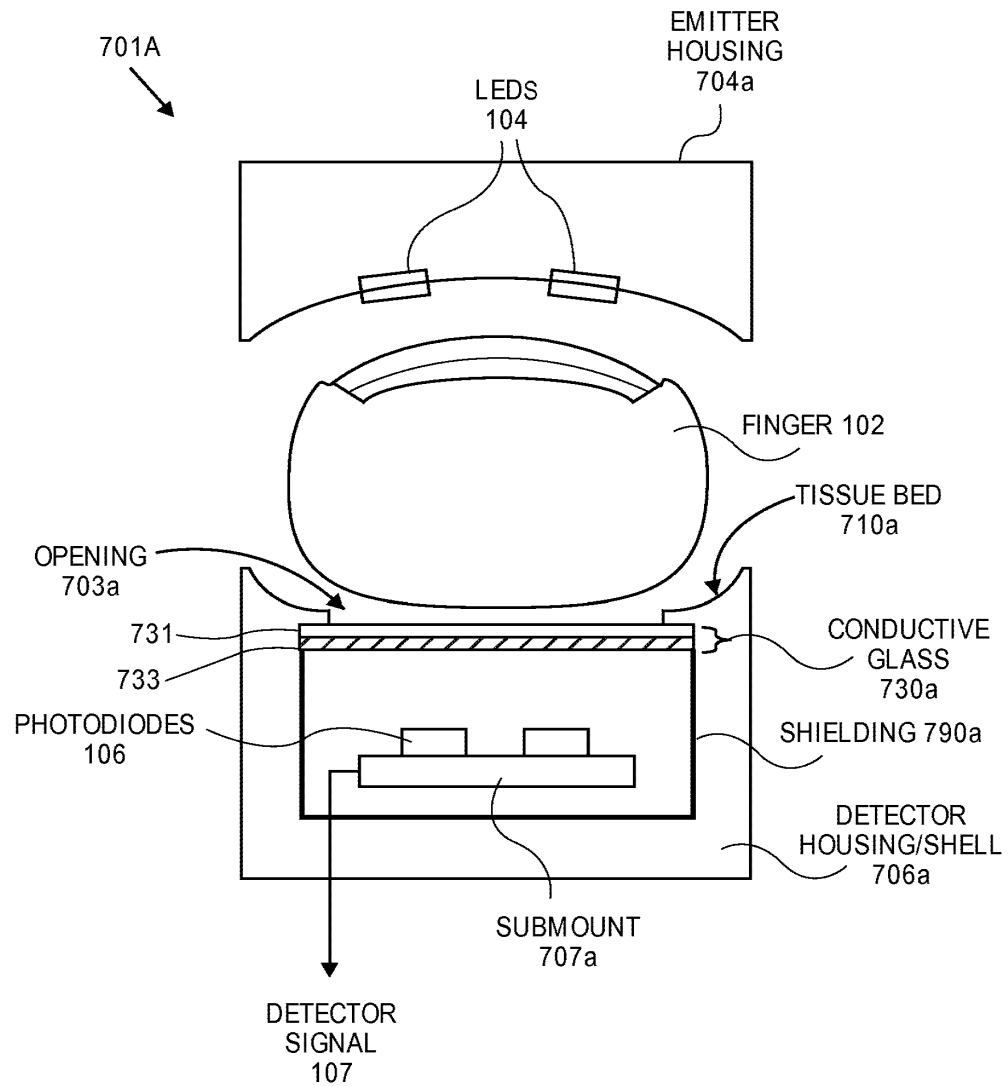
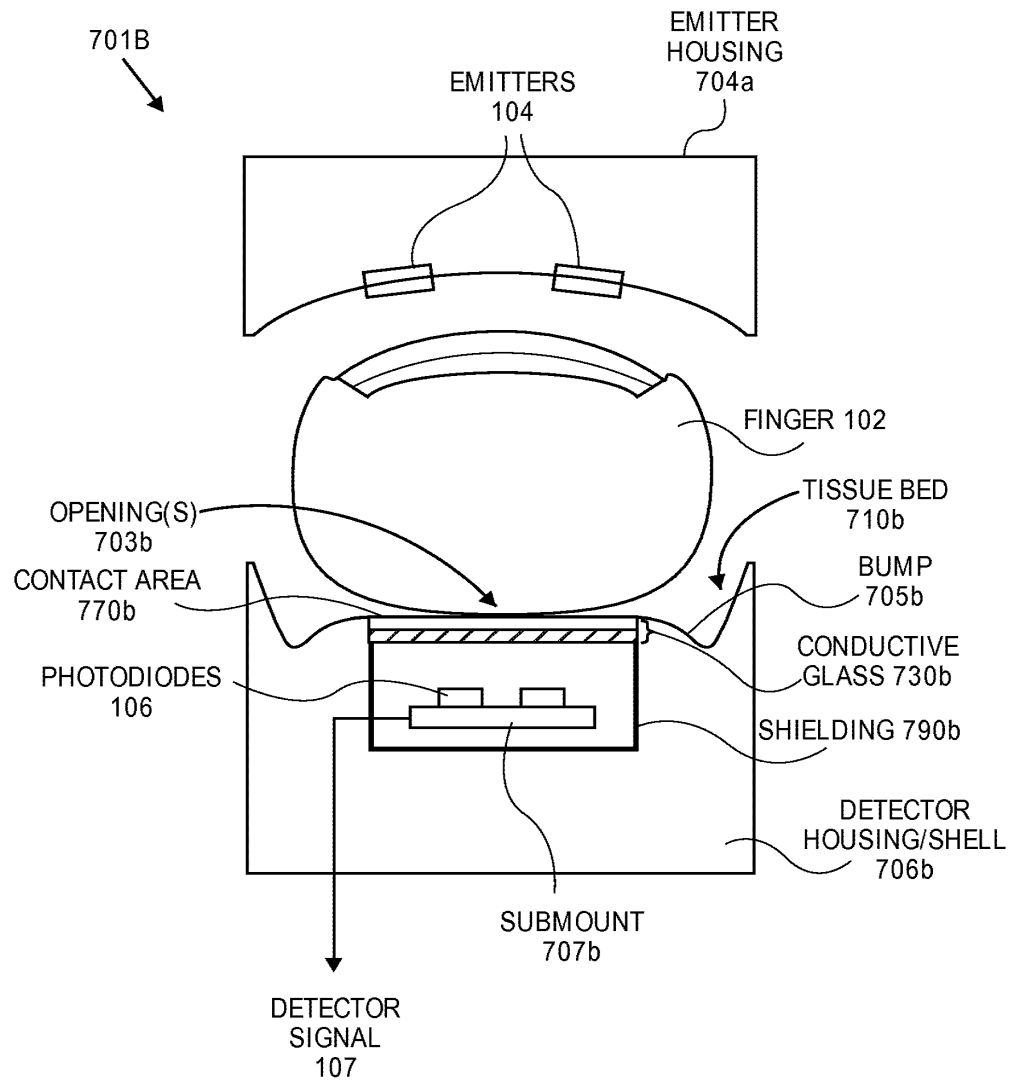


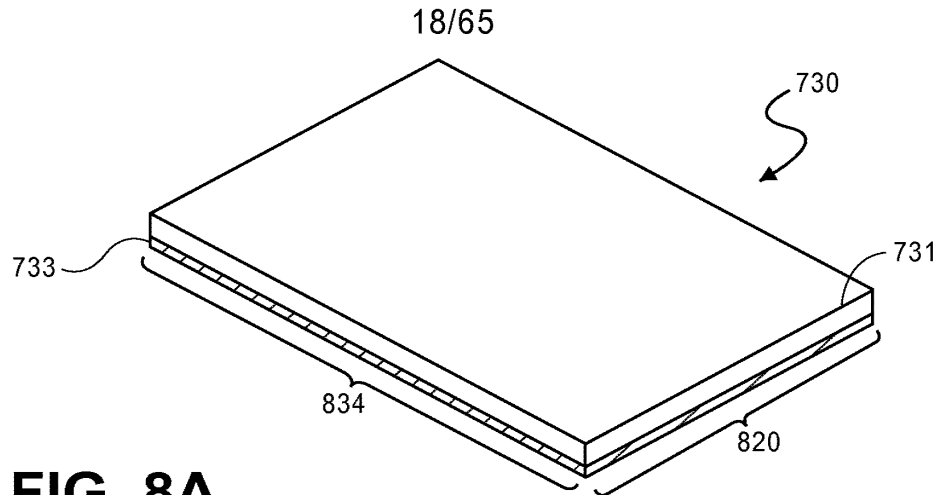
FIG. 6E

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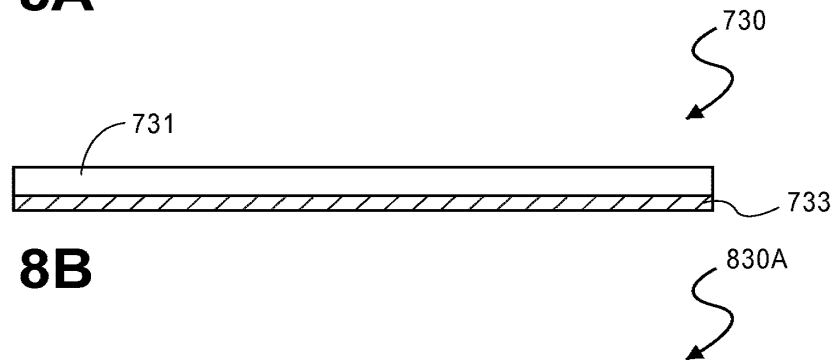
**FIG. 7A**

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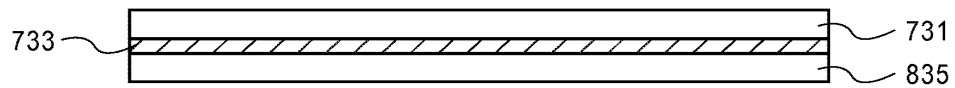
**FIG. 7B**



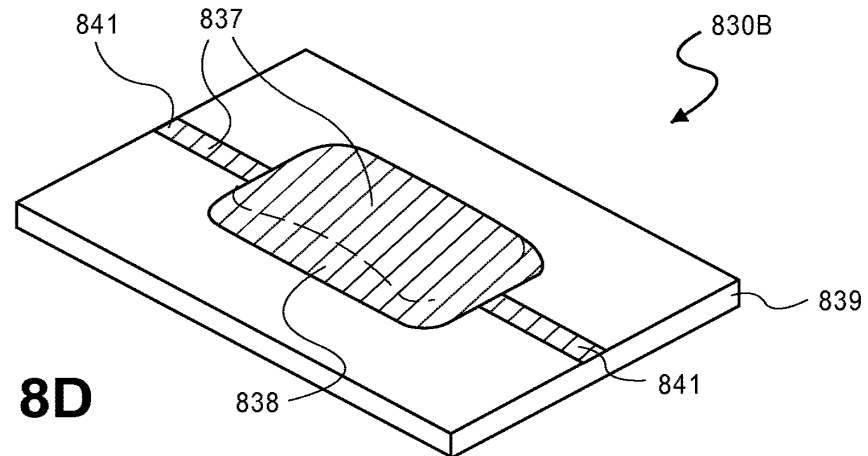
**FIG. 8A**



**FIG. 8B**



**FIG. 8C**



**FIG. 8D**

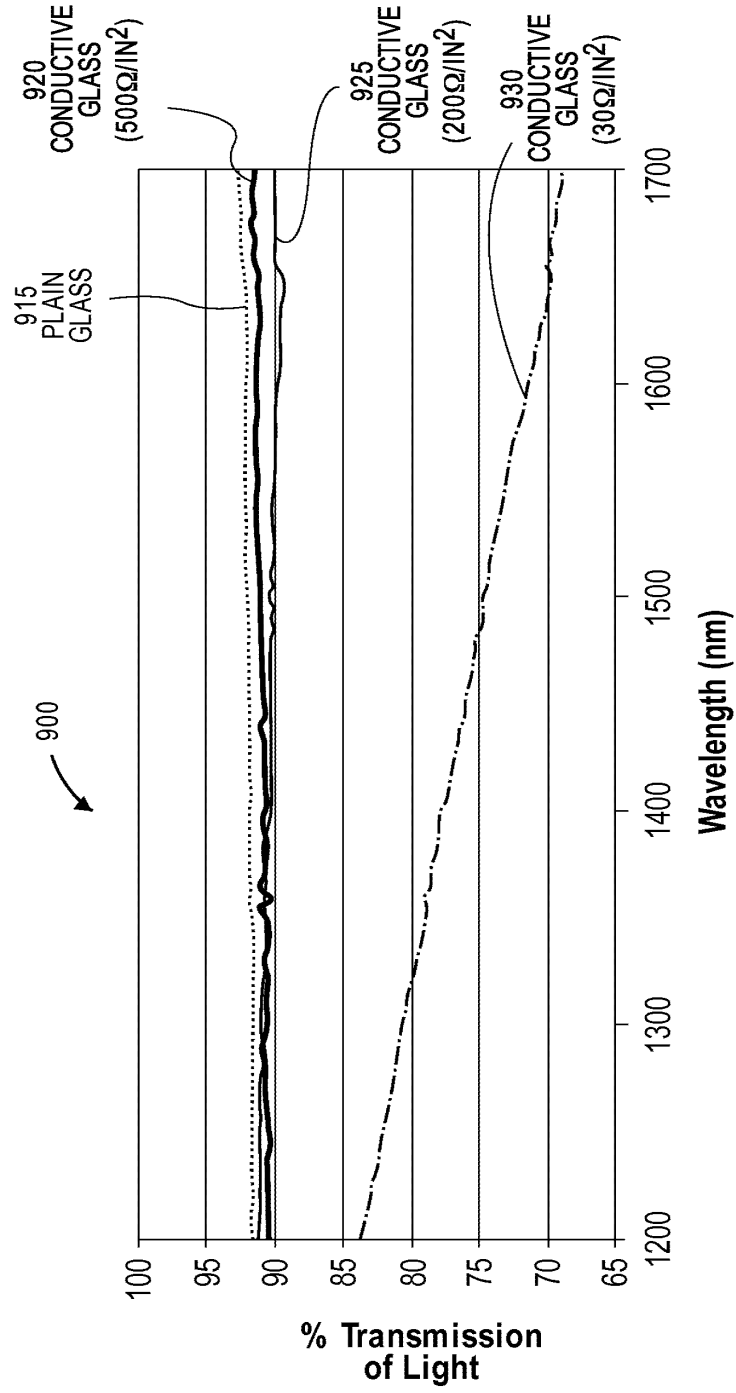
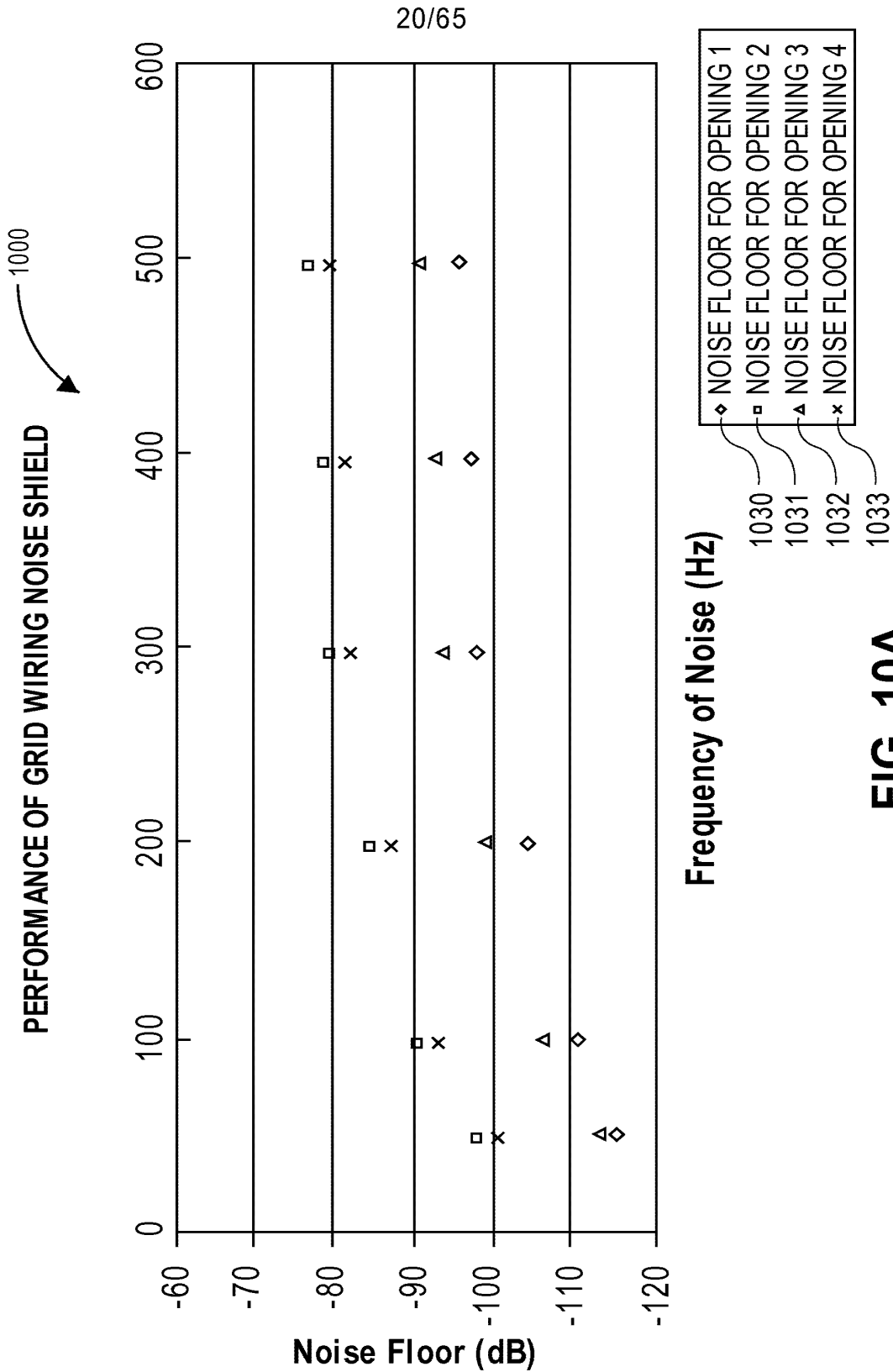
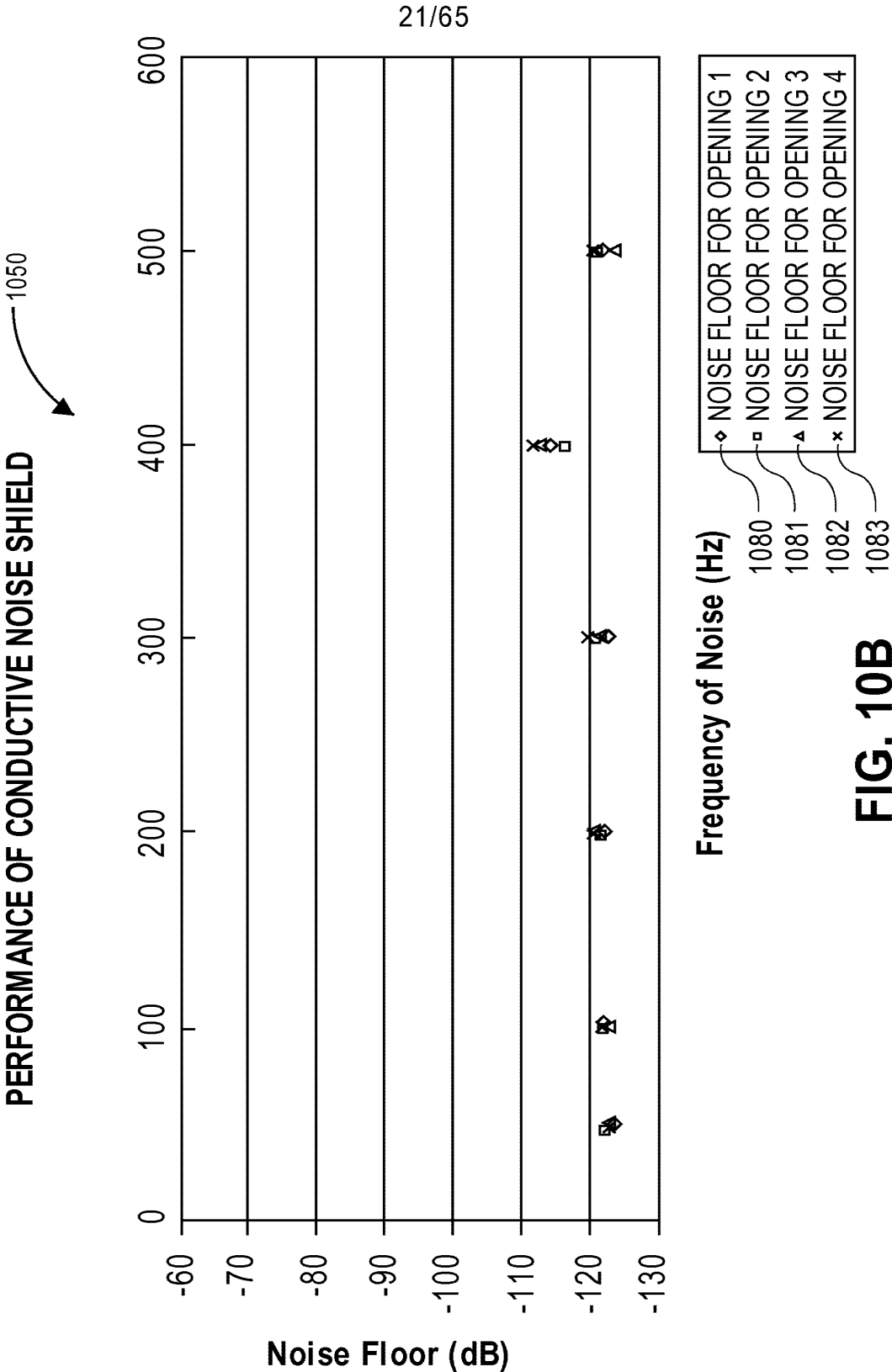


FIG. 9

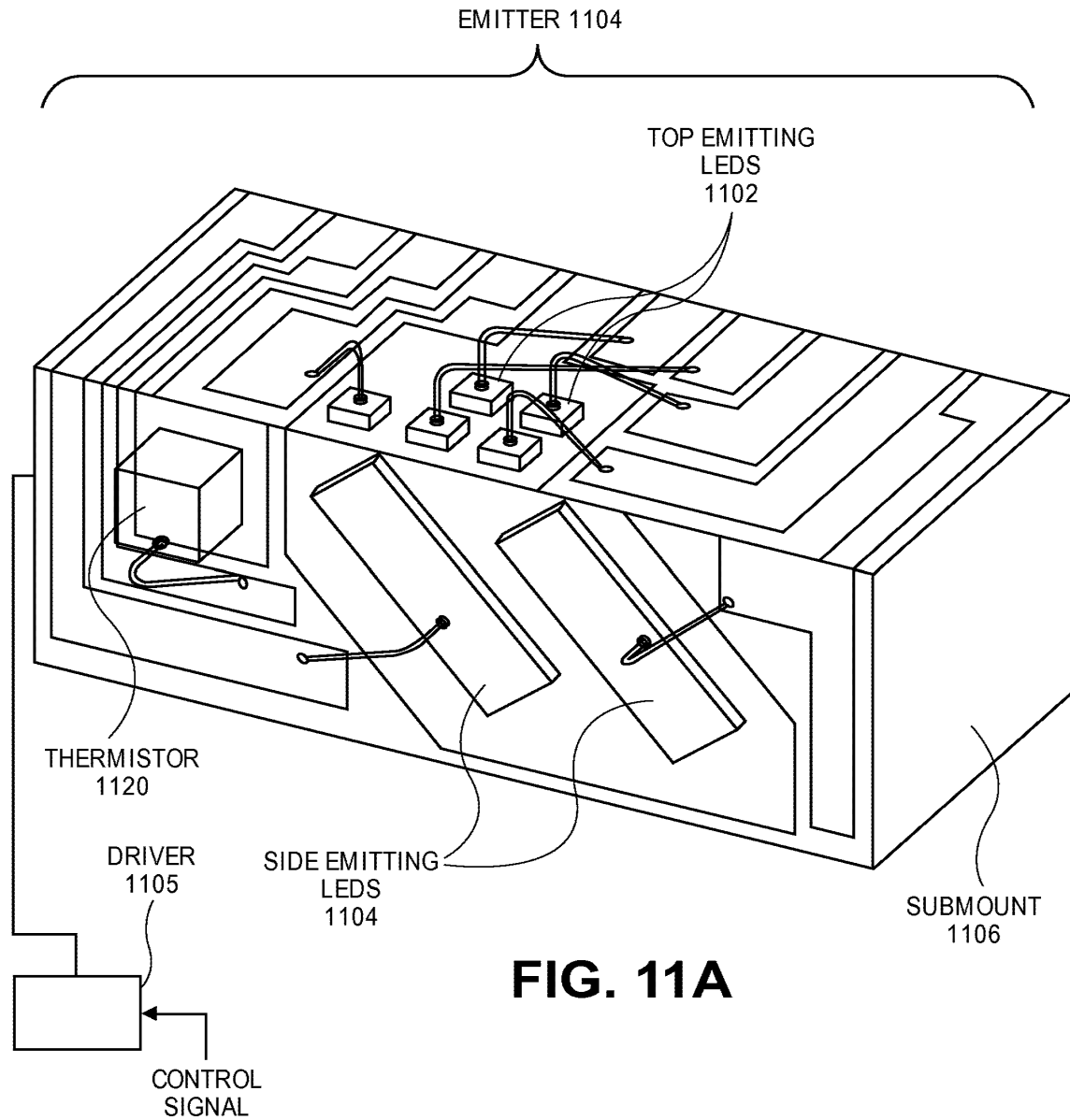


**FIG. 10A**

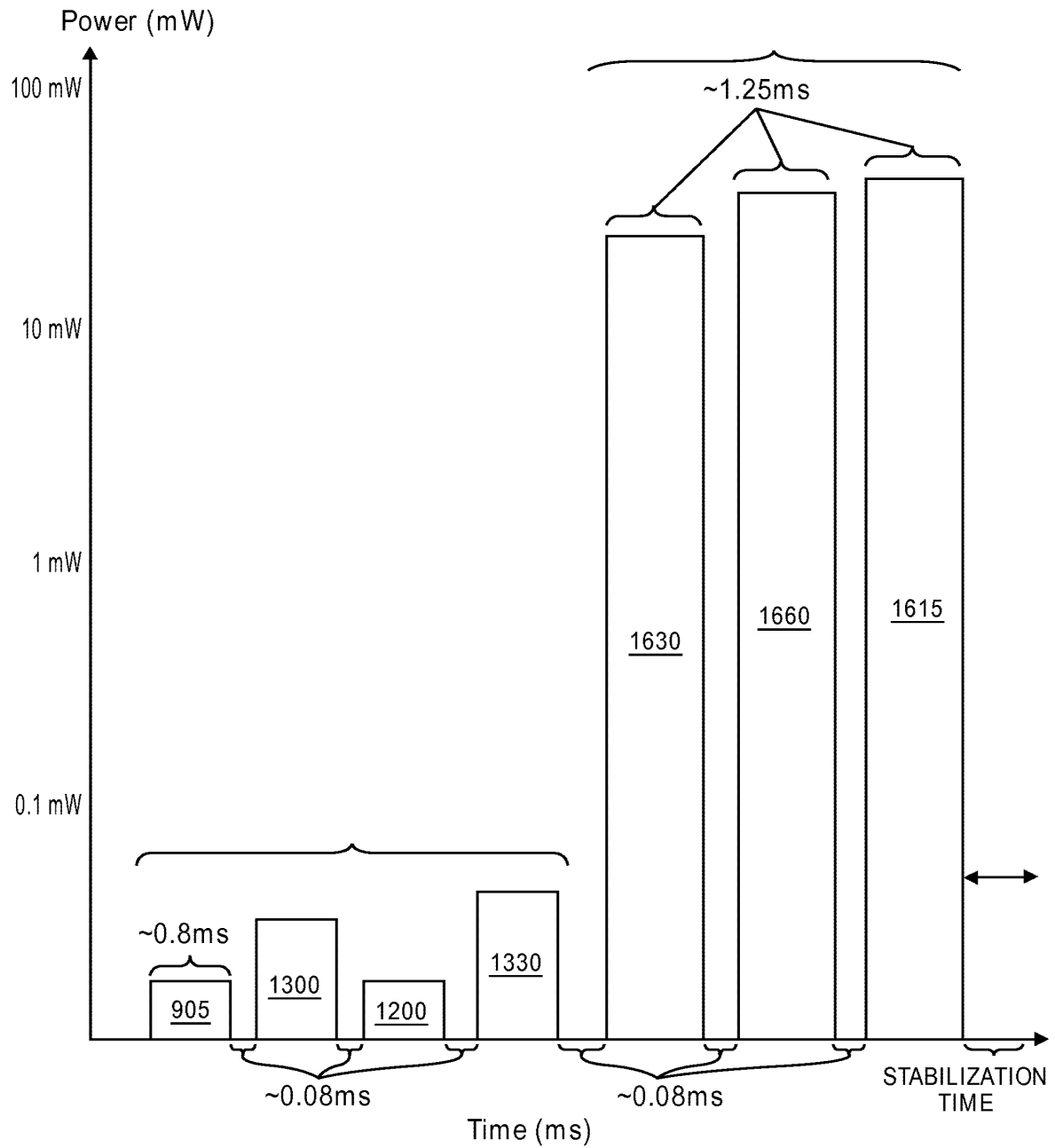




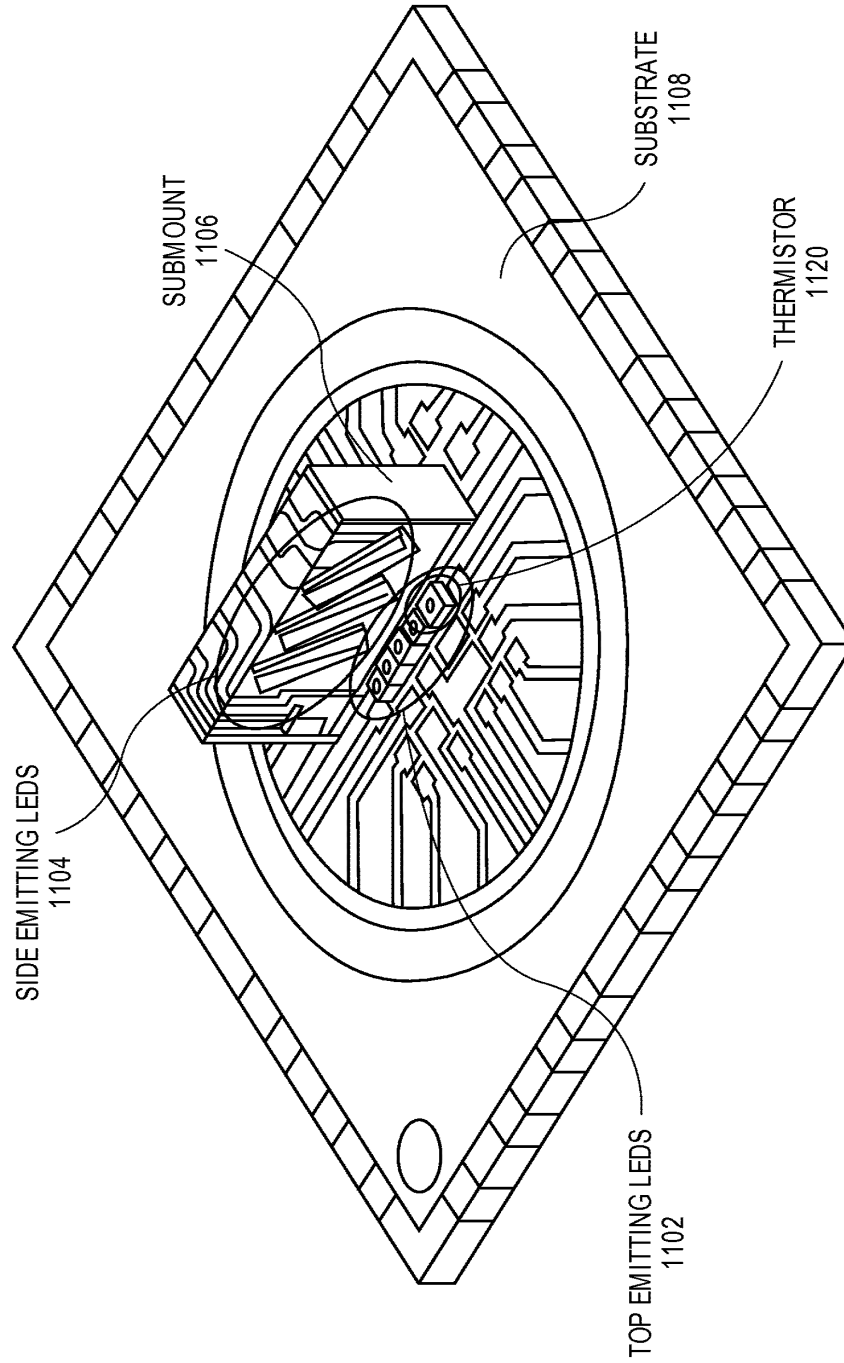
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**FIG. 11B**

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**FIG. 11C**

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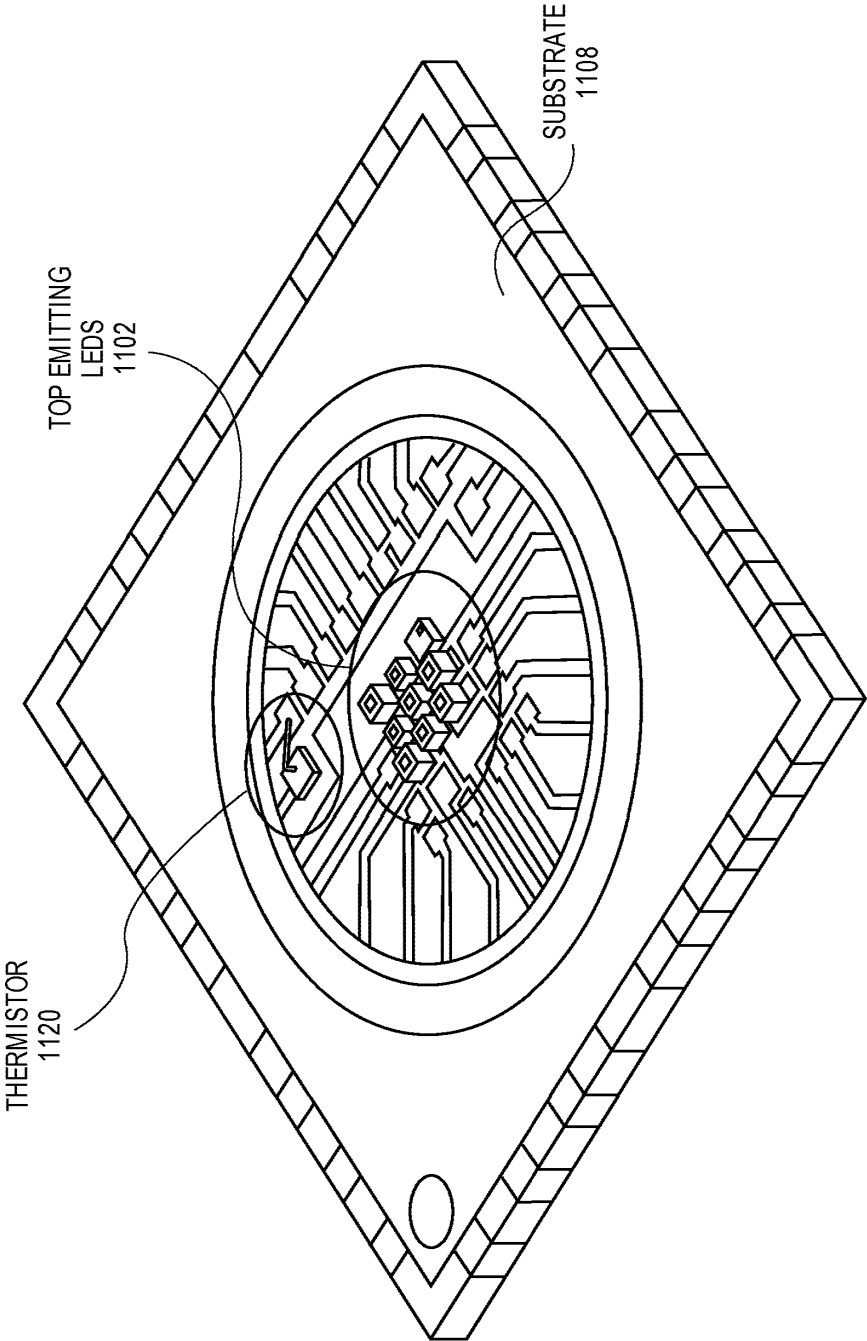
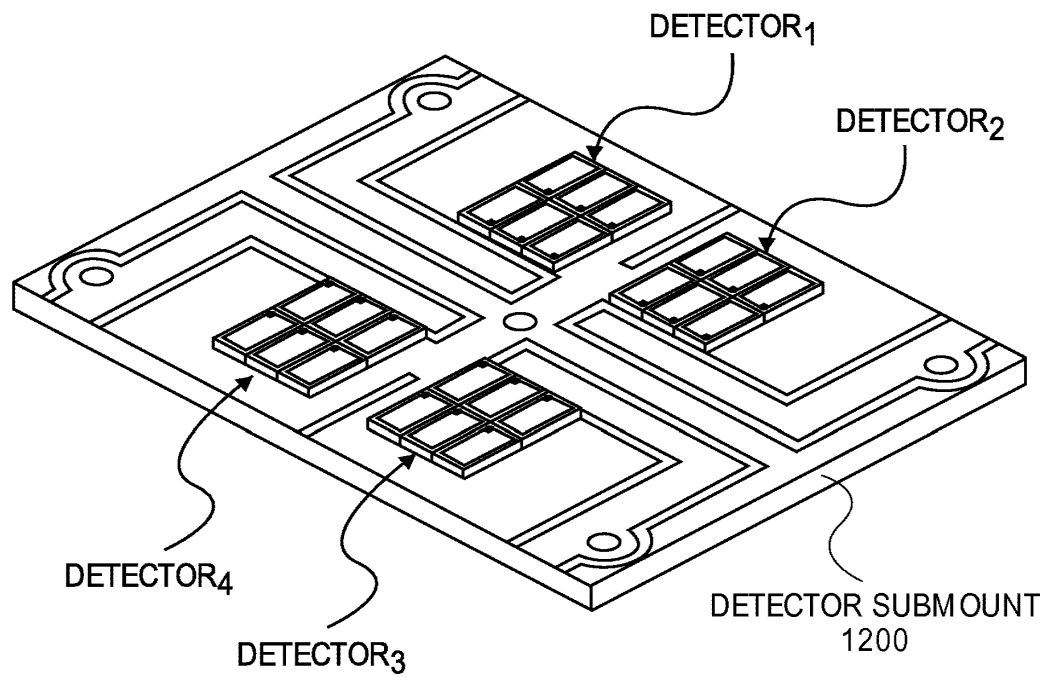


FIG. 11D

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**FIG. 12A**

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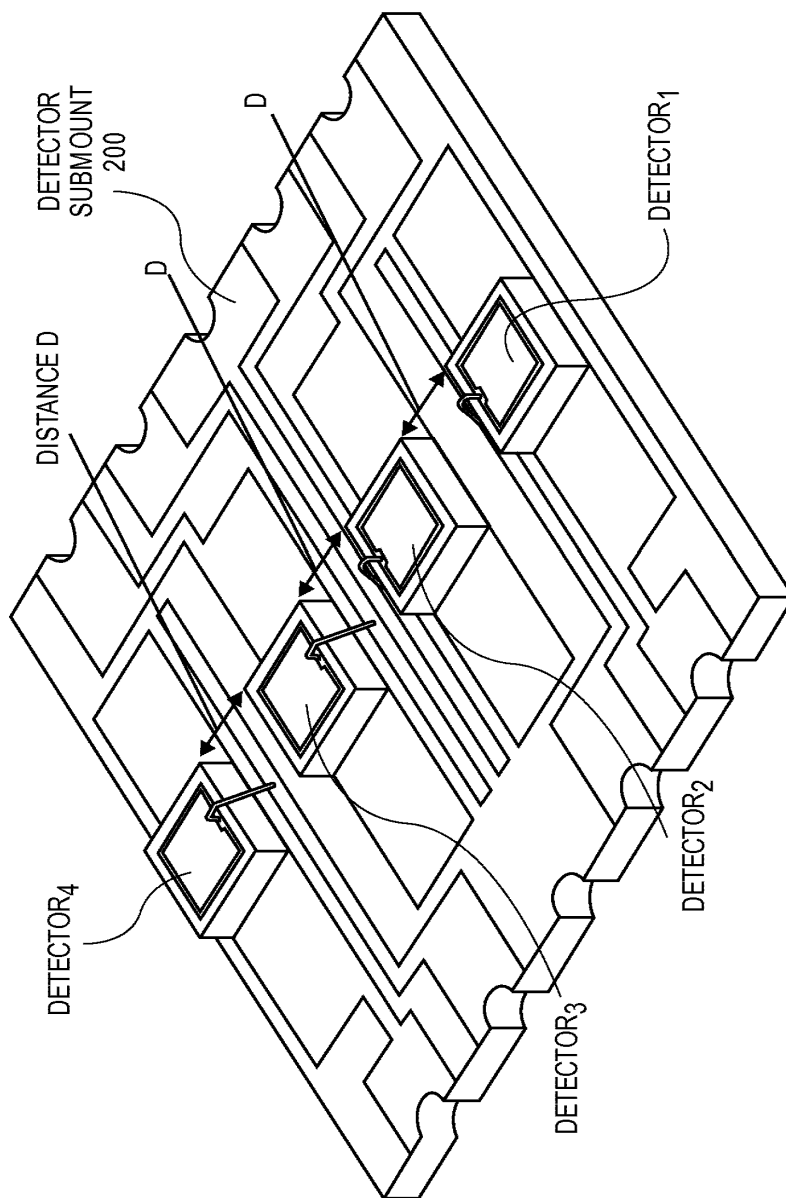
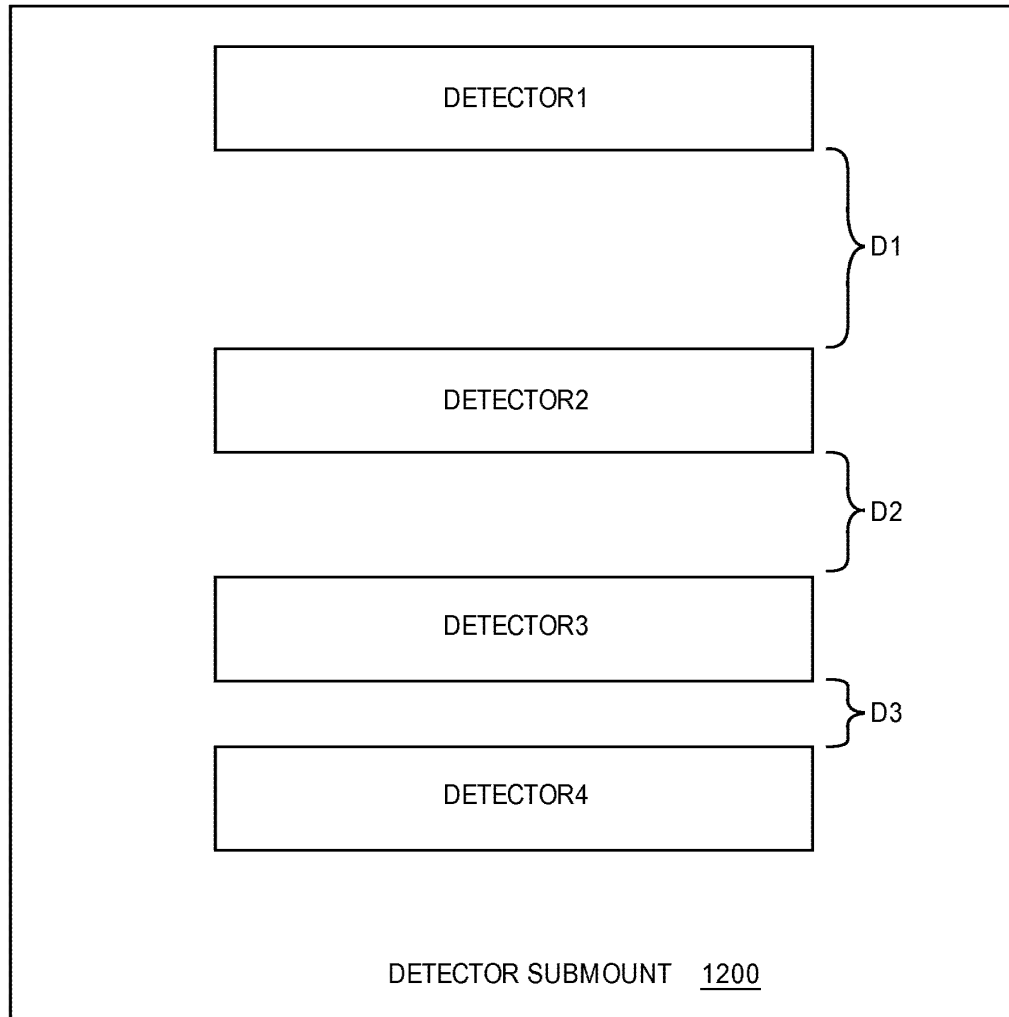


FIG. 12B

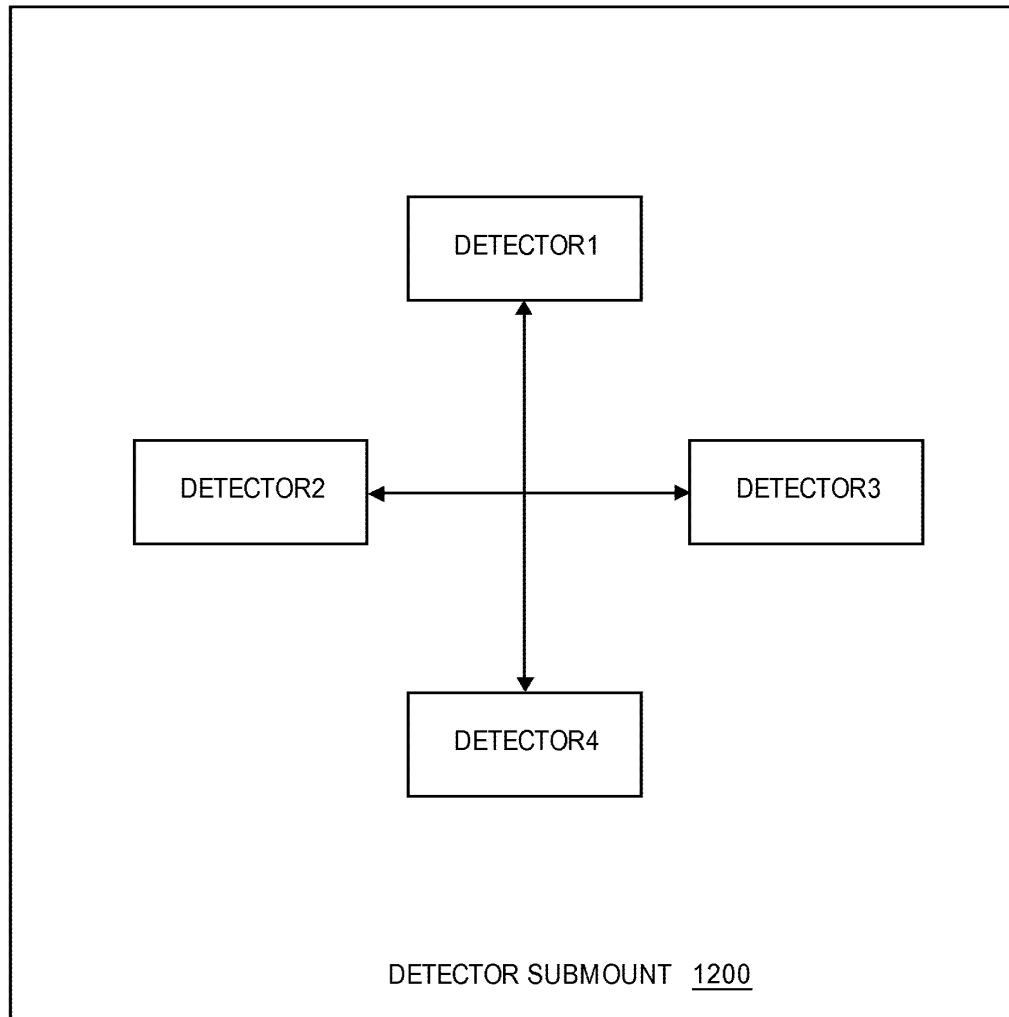
Appx58233

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**FIG. 12C**

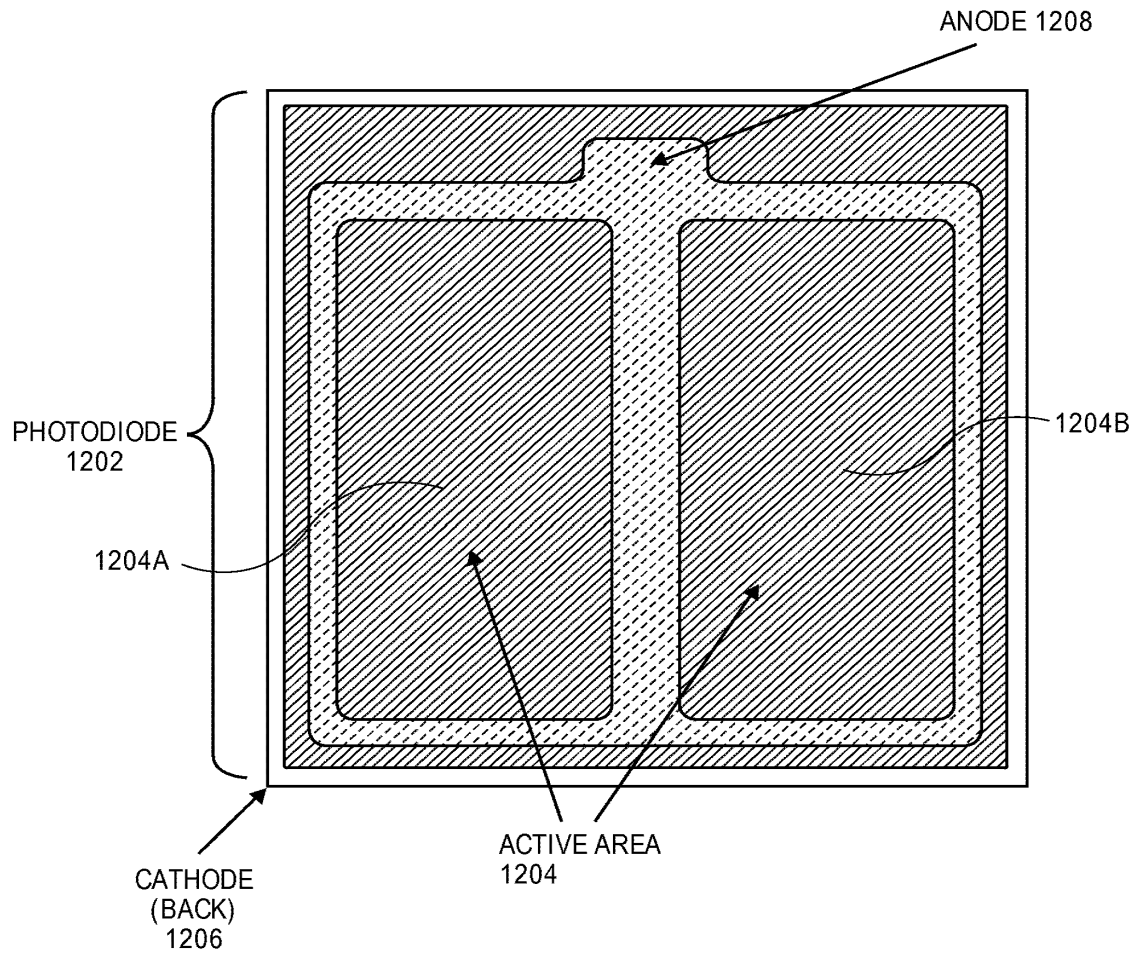
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**FIG. 12D**

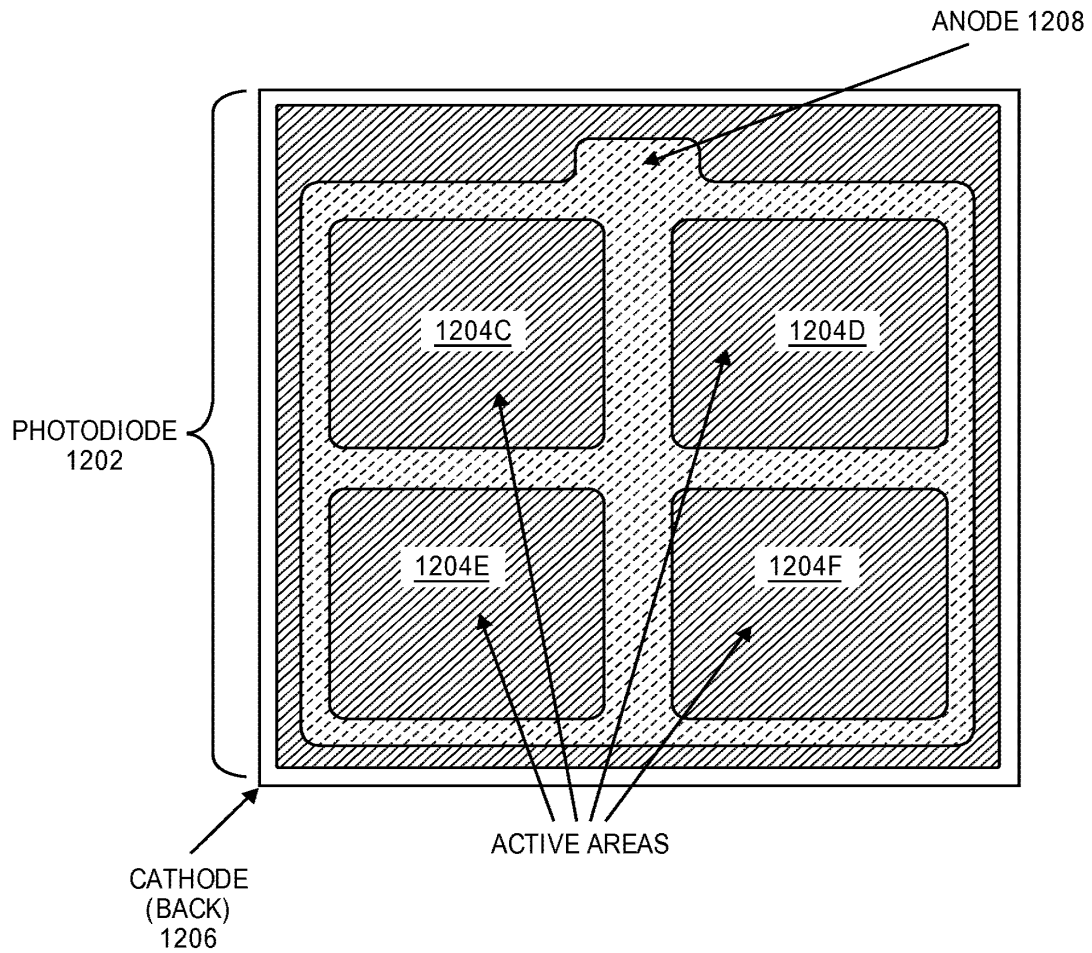


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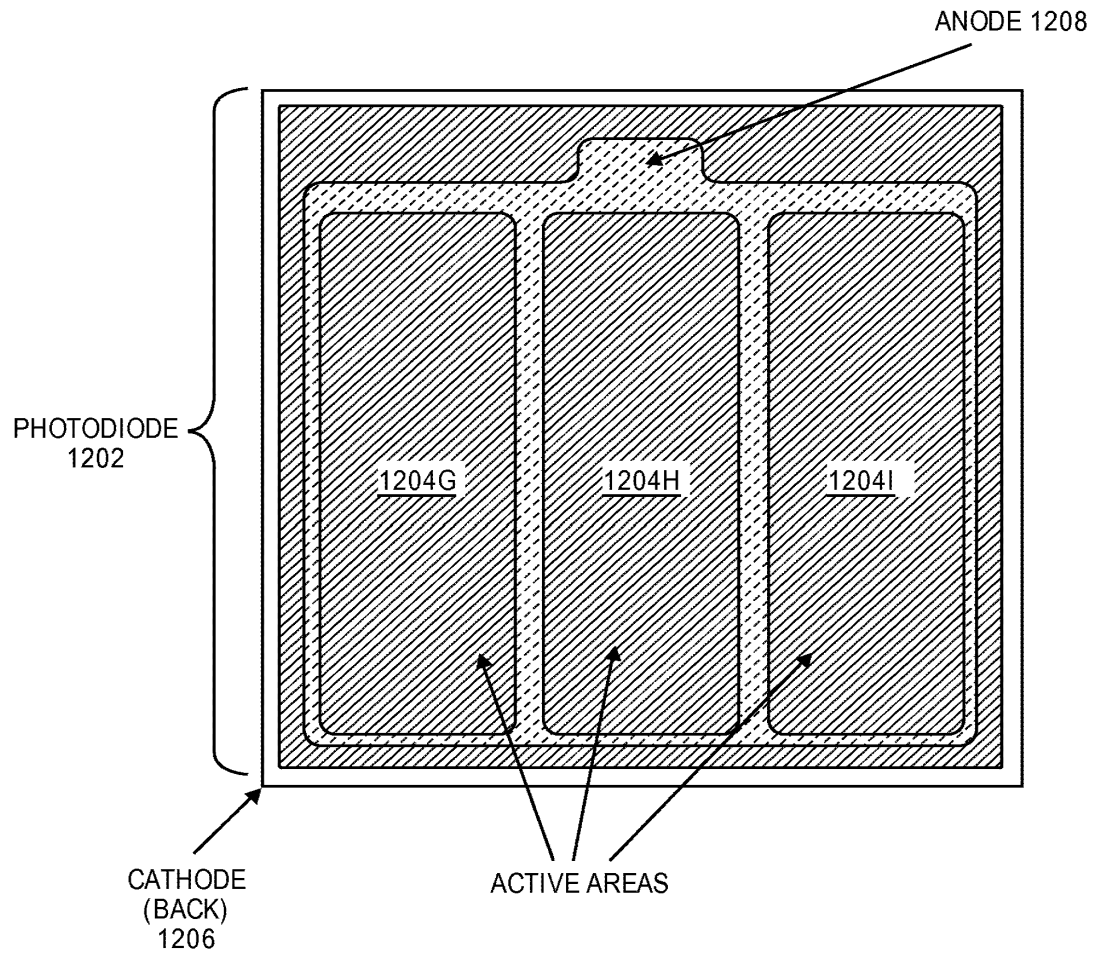
**FIG. 12E**

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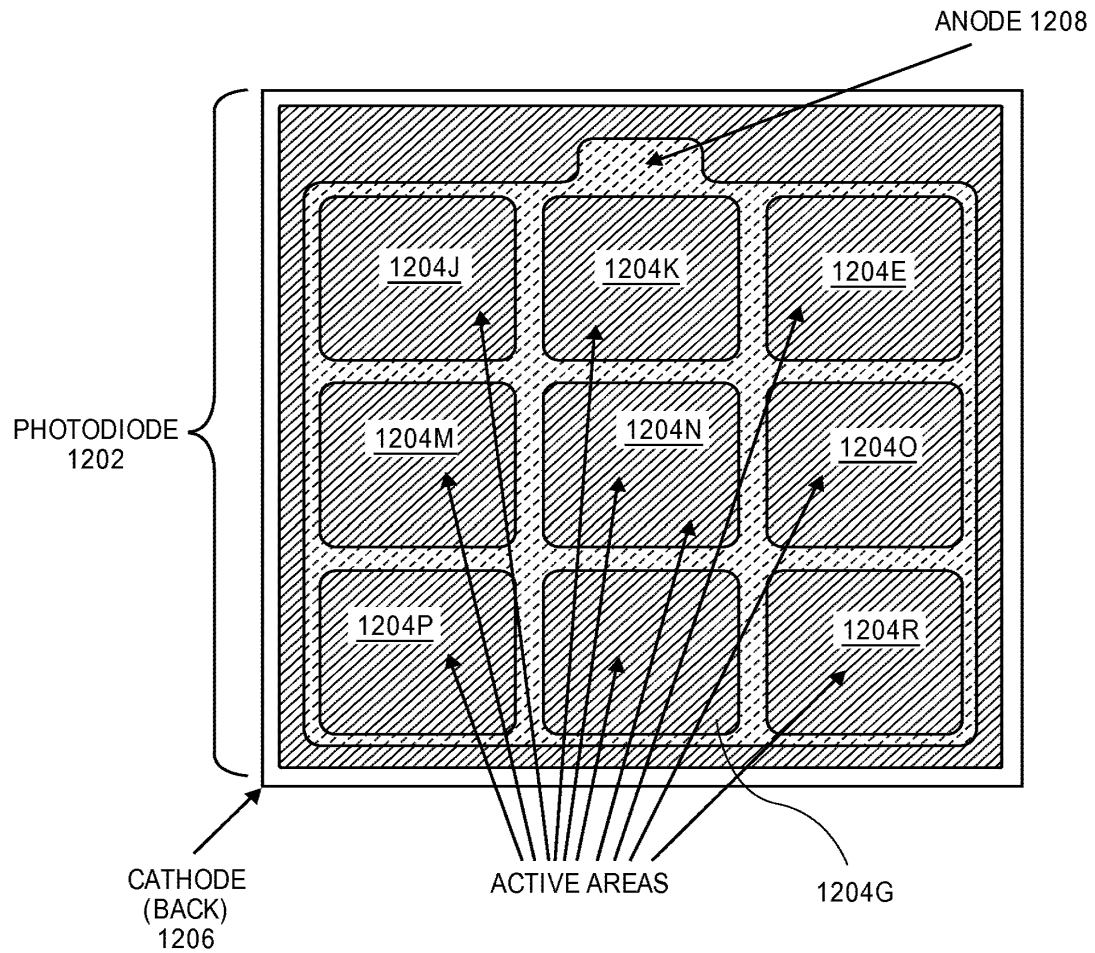
**FIG. 12F**

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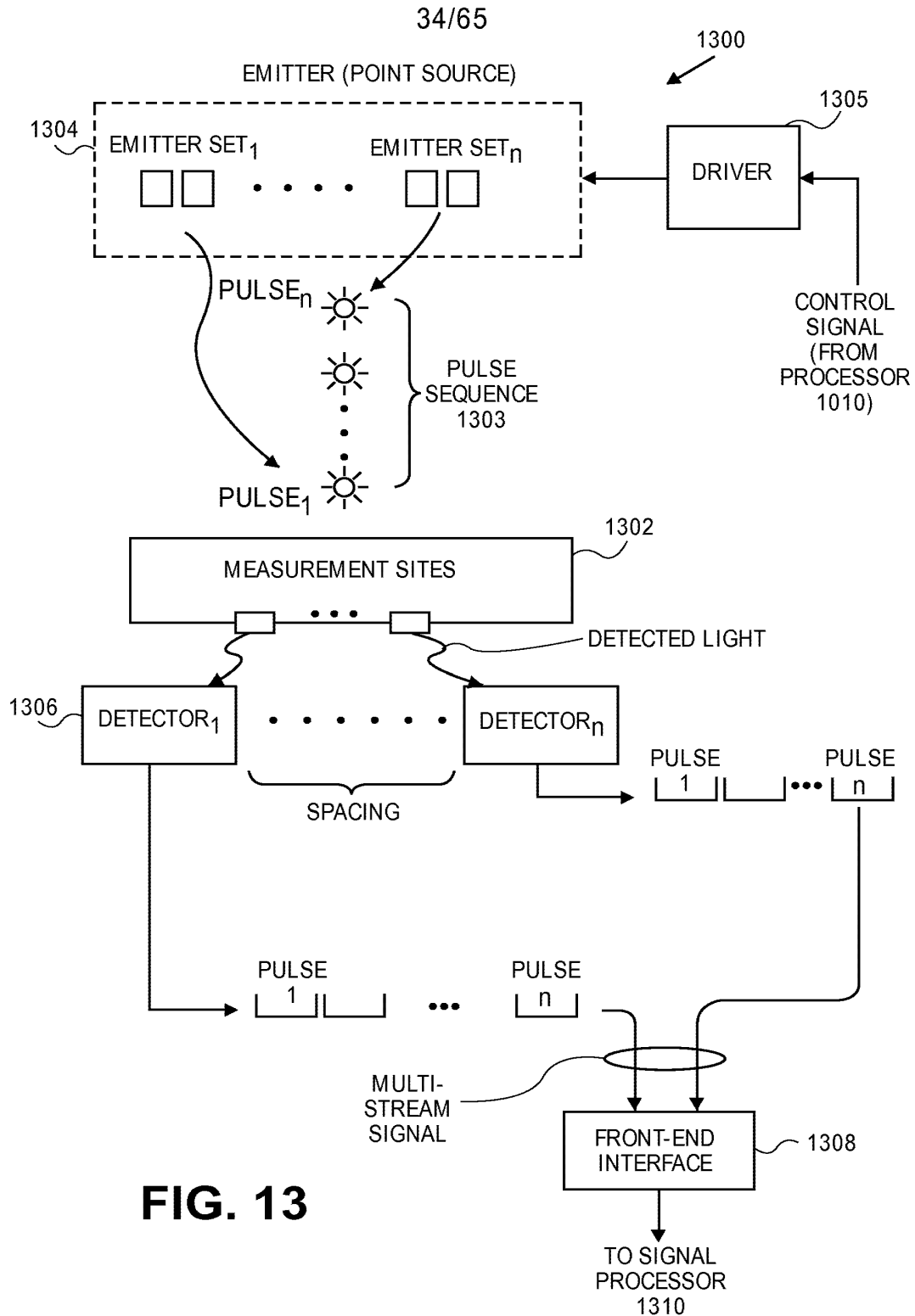


**FIG. 12G**

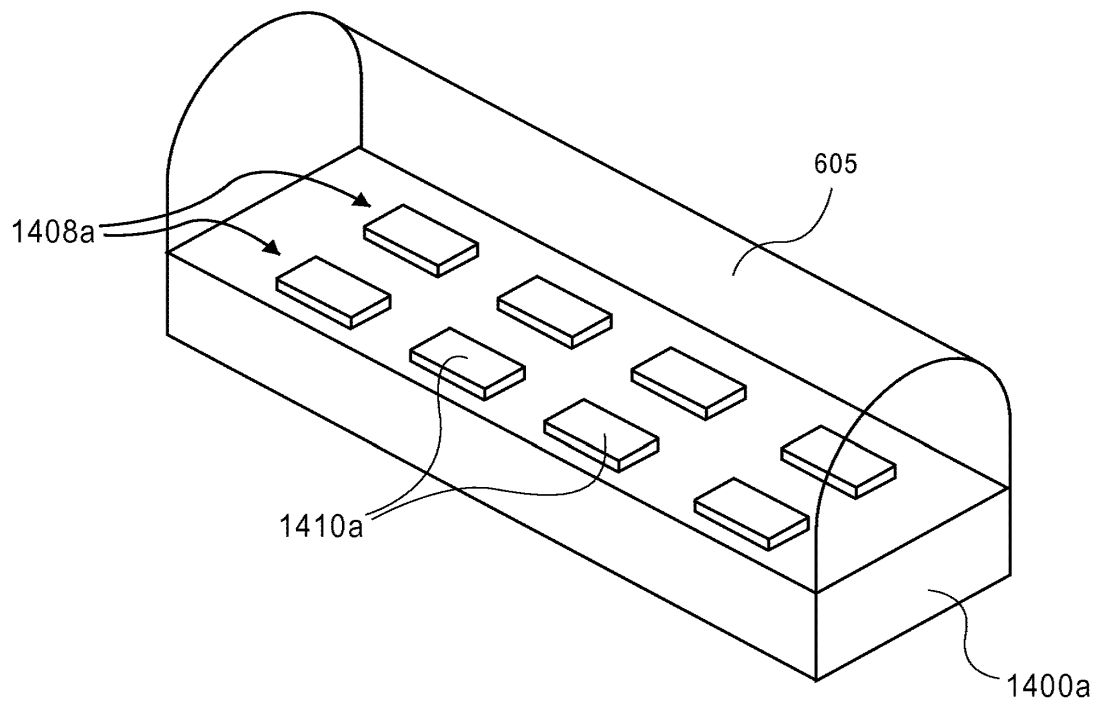
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**FIG. 12H**

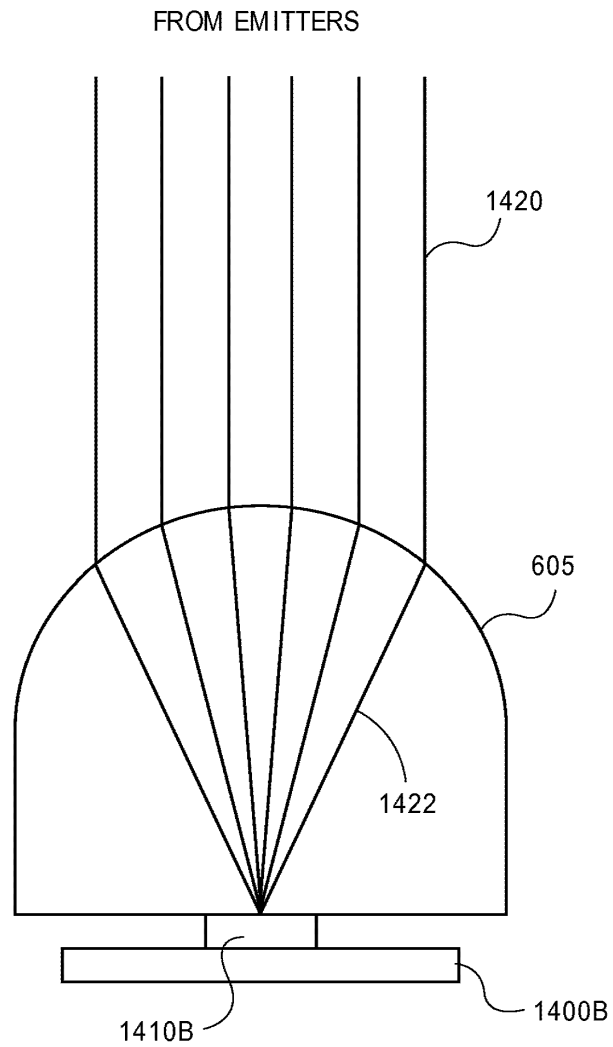


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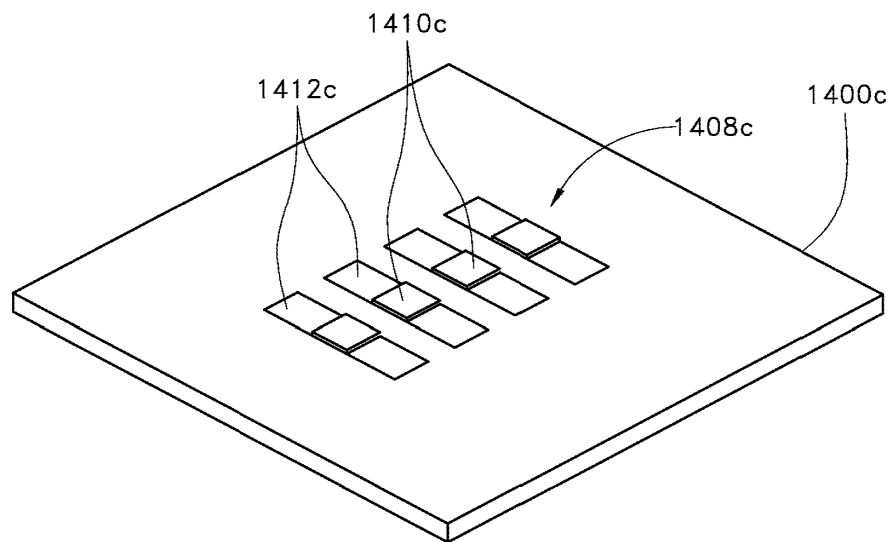
**FIG. 14A**

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**FIG. 14B**

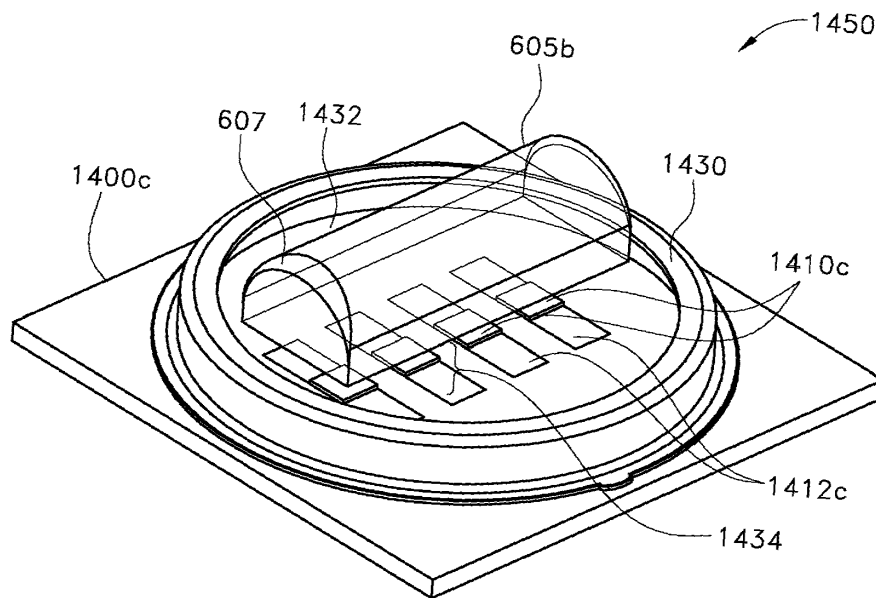
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**FIG. 14C**

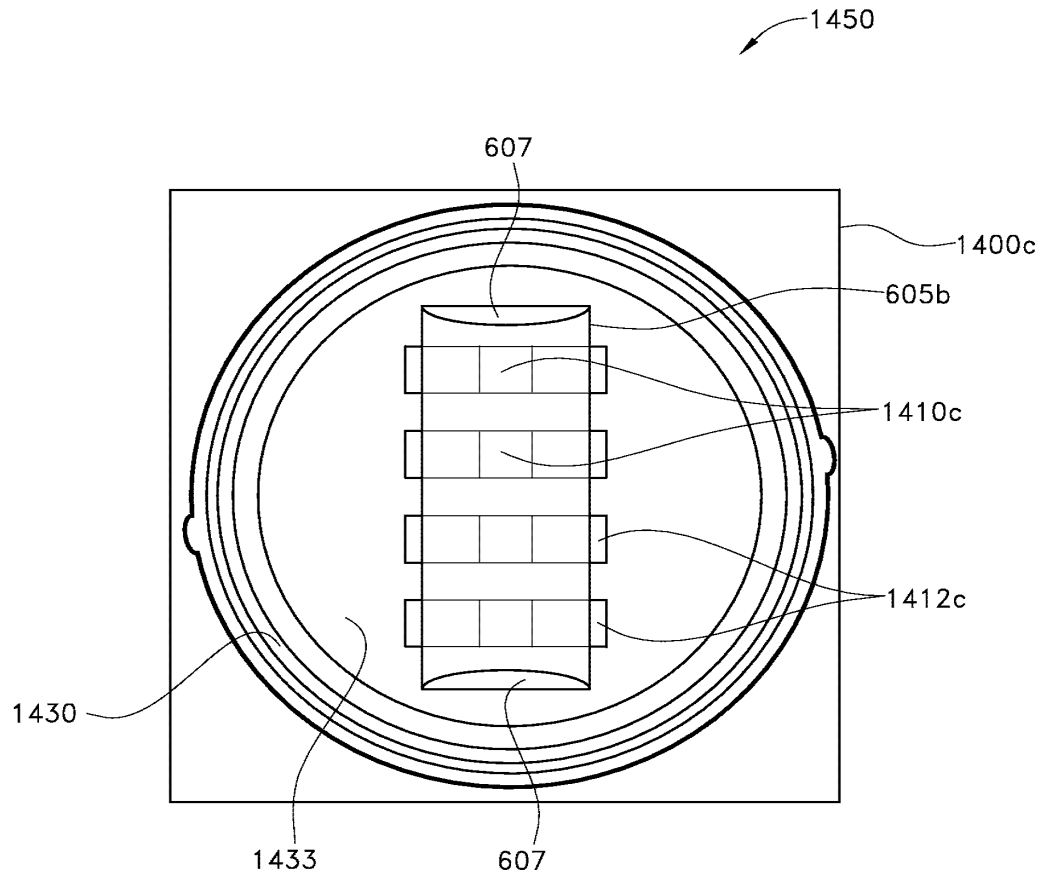


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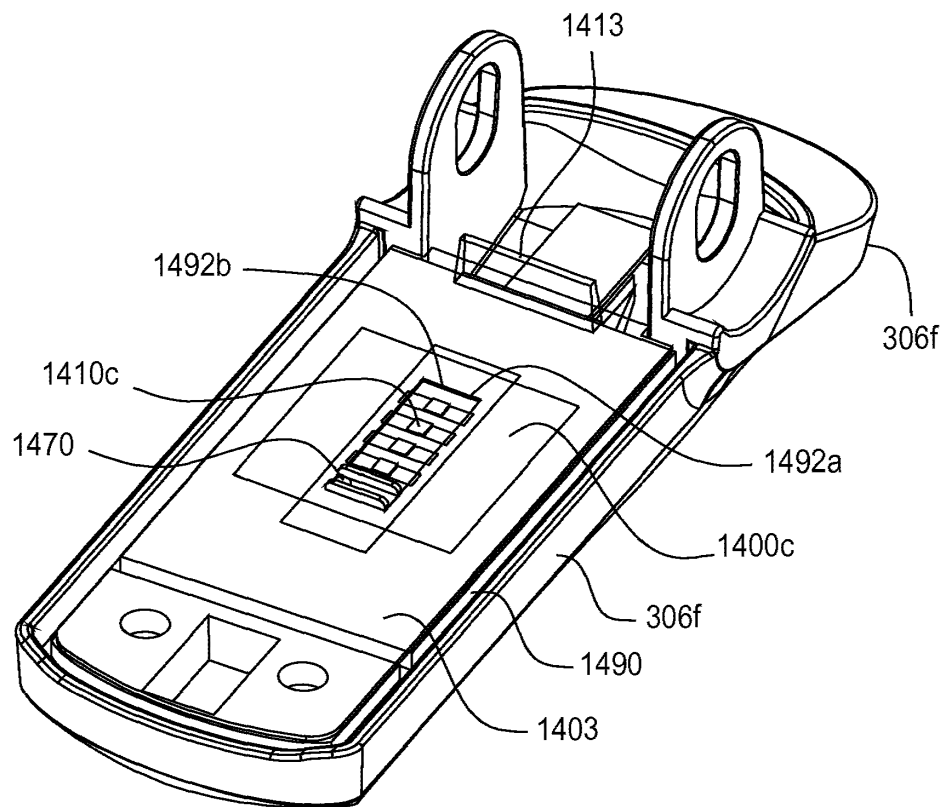
**FIG. 14D**

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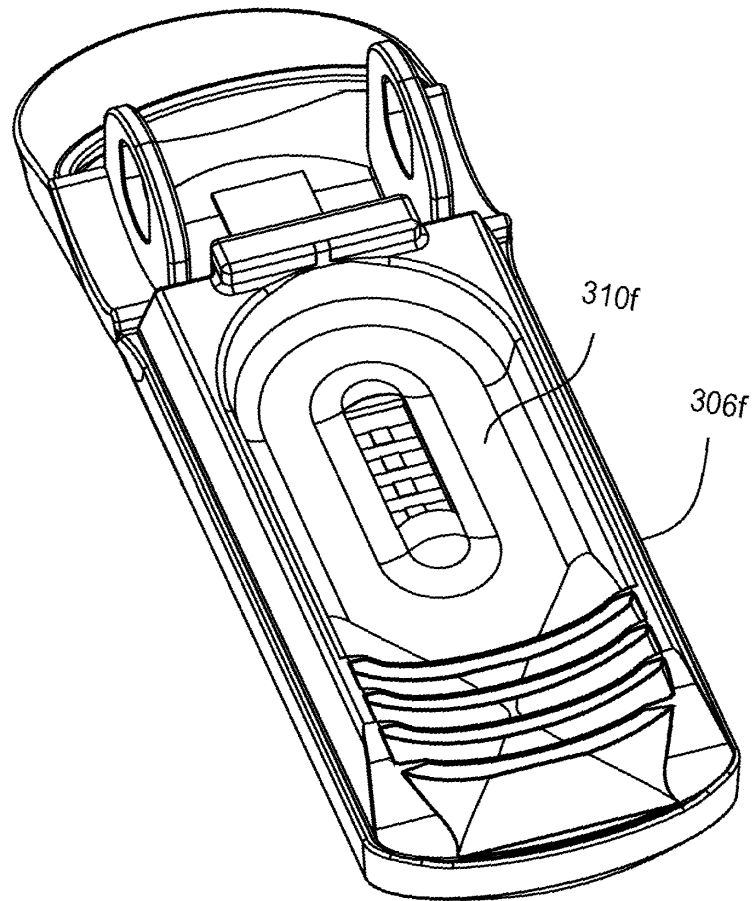
**FIG. 14E**

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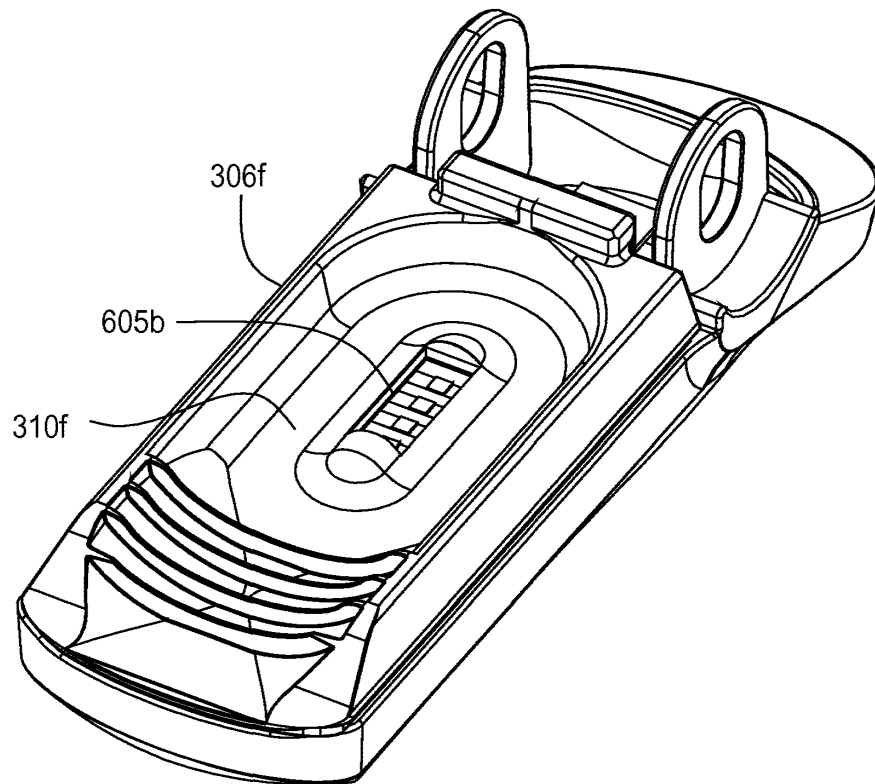
**FIG. 14F**

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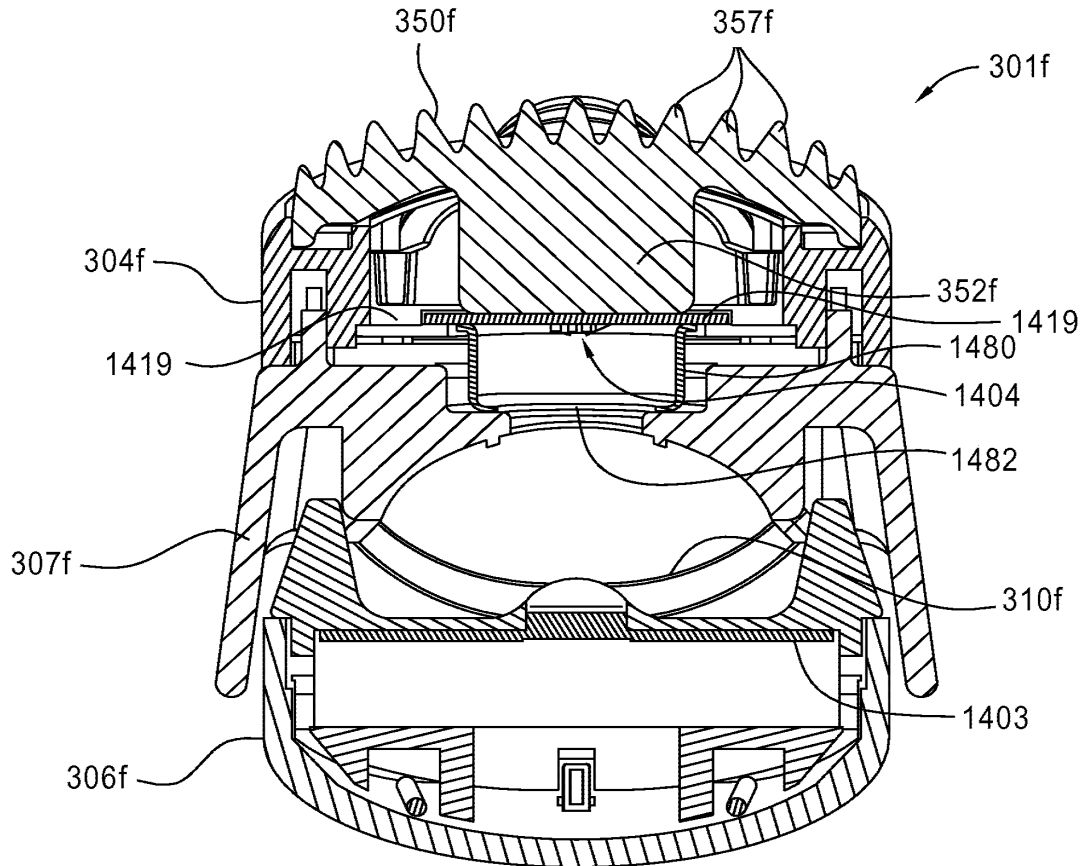
**FIG. 14G**

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**FIG. 14H**

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**FIG. 14I**

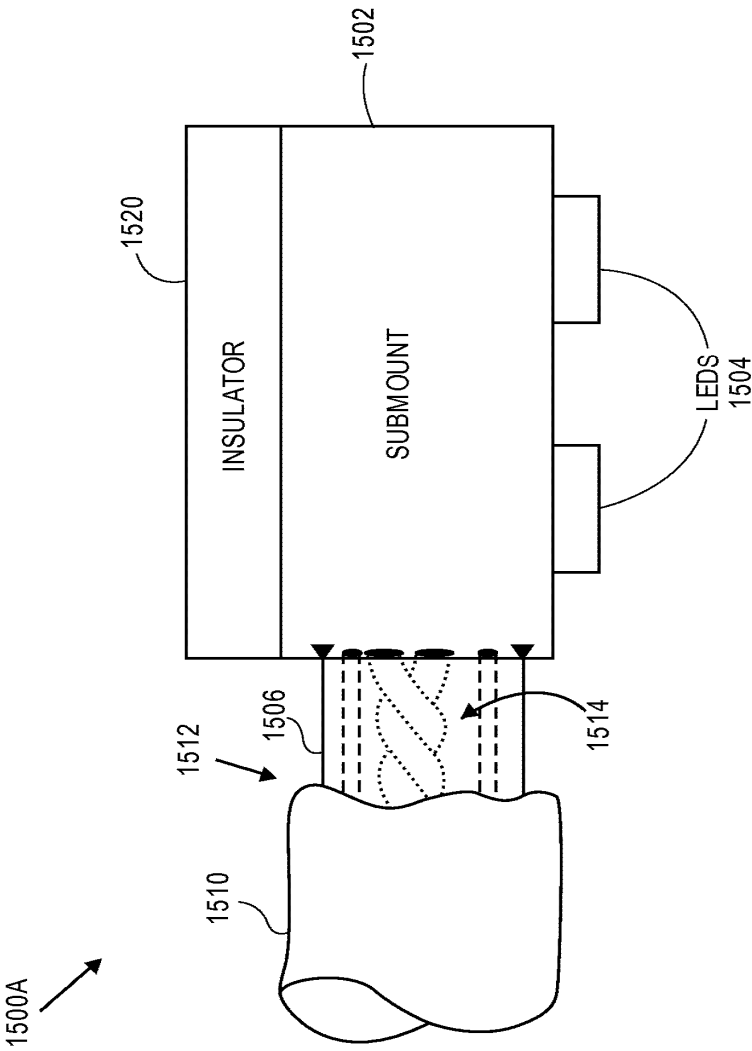
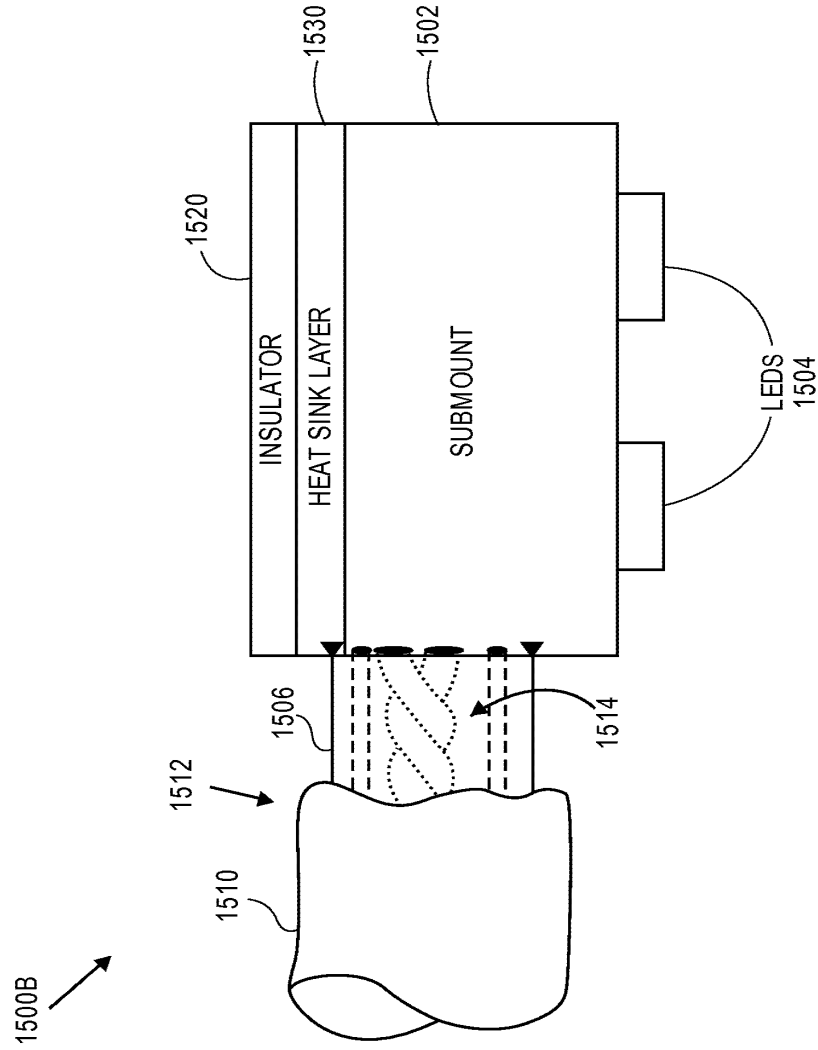


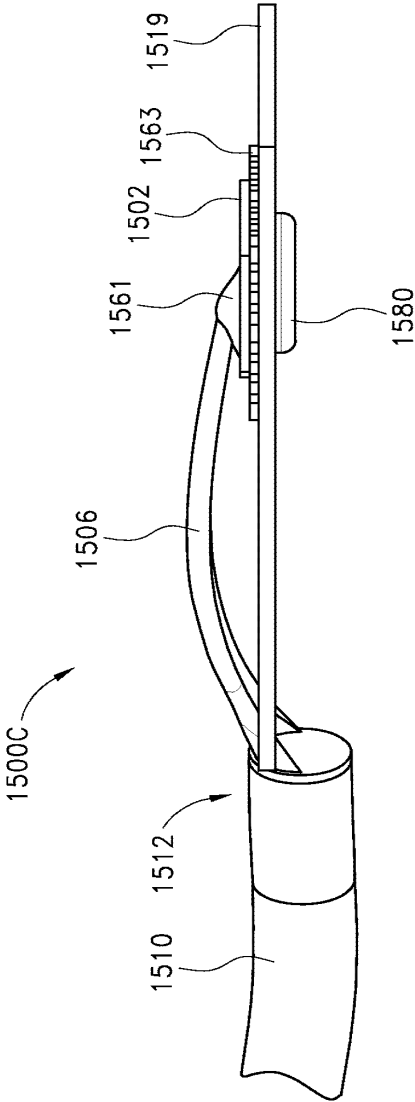
FIG. 15A

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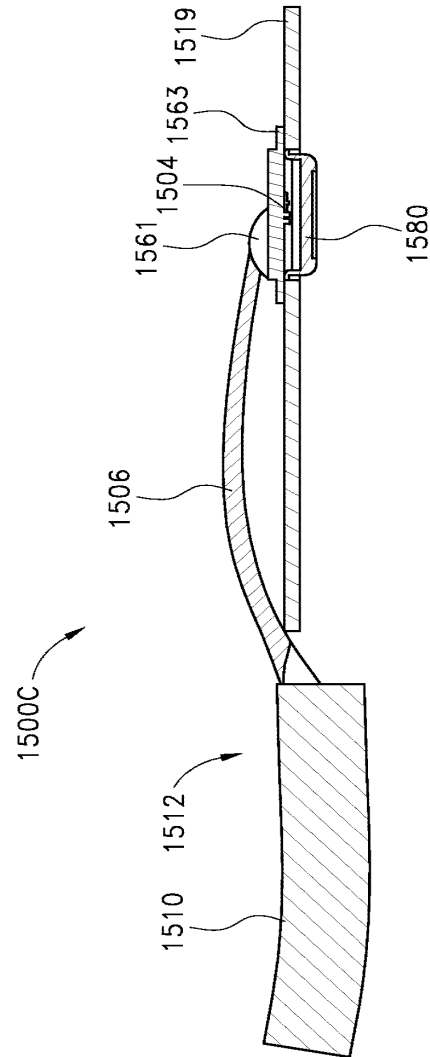
**FIG. 15B**



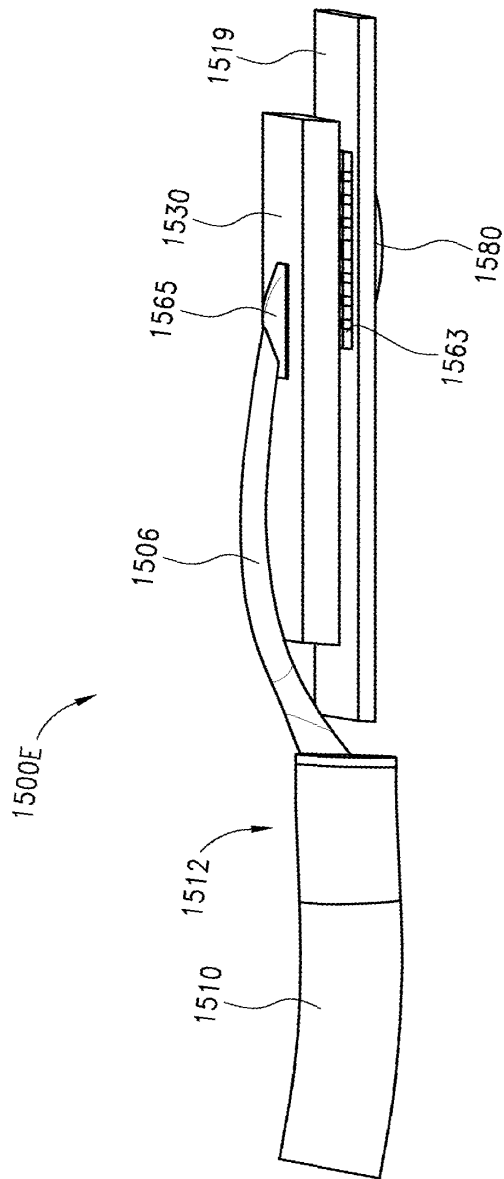


**FIG. 15C**

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**FIG. 15D**



**FIG. 15E**

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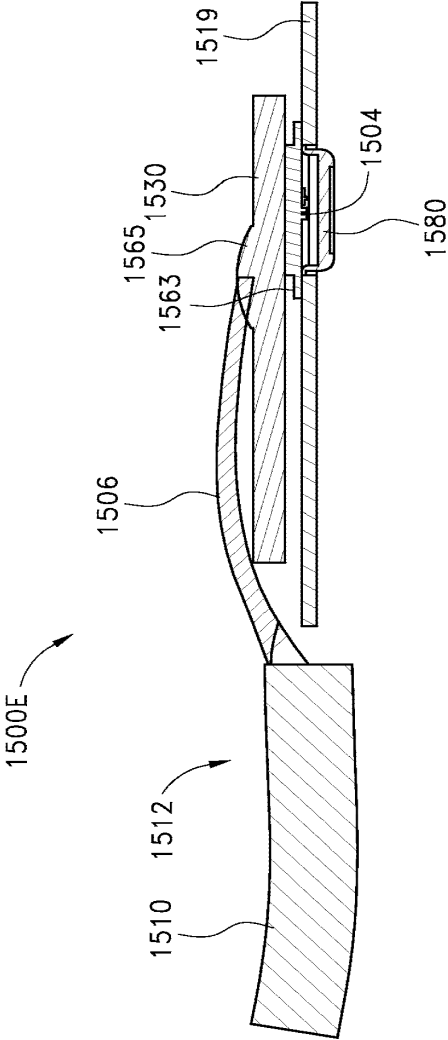
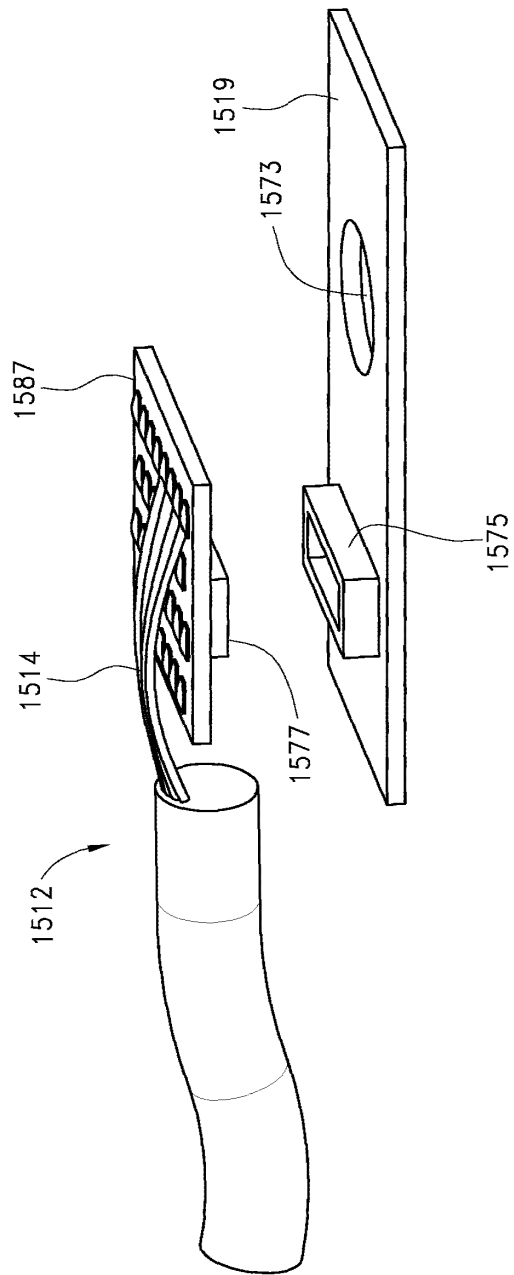


FIG. 15F



**FIG. 15G**

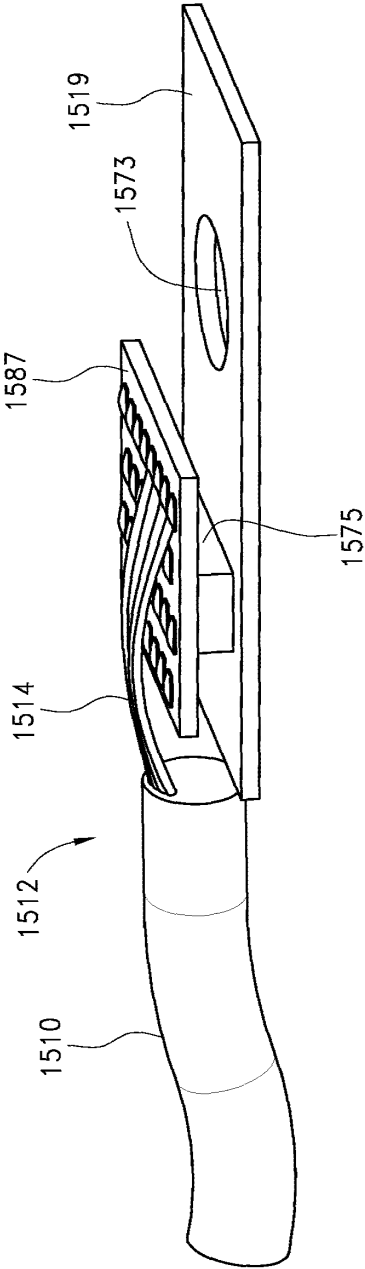


FIG. 15H

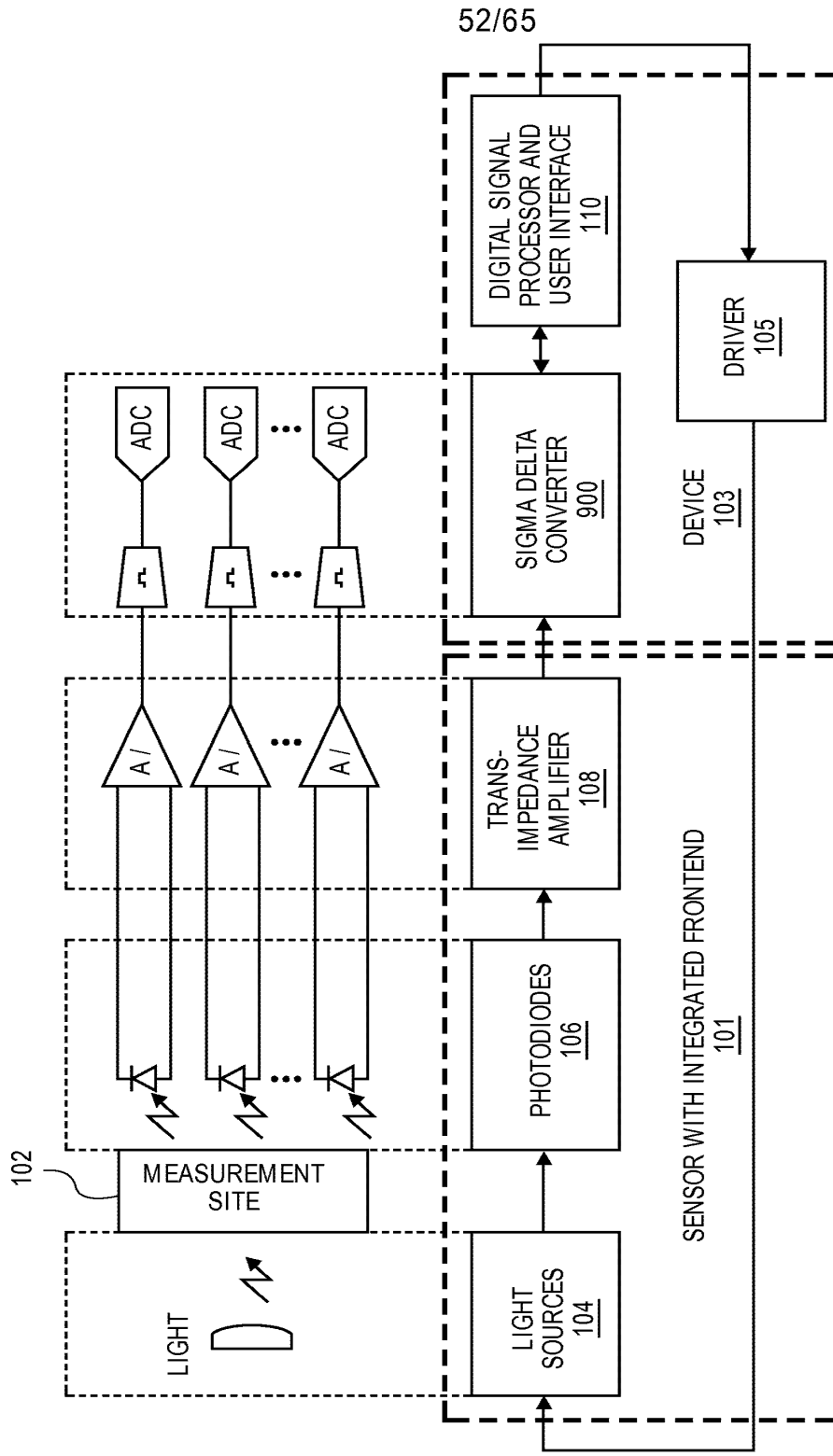
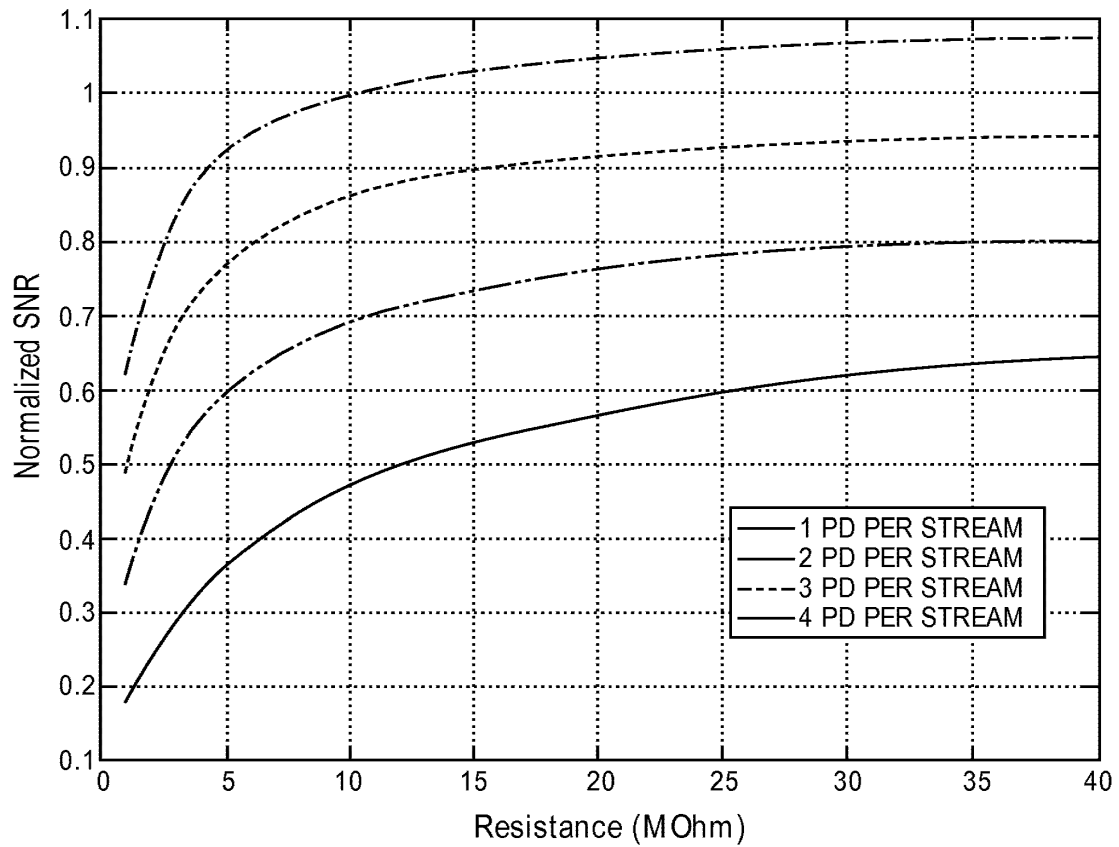
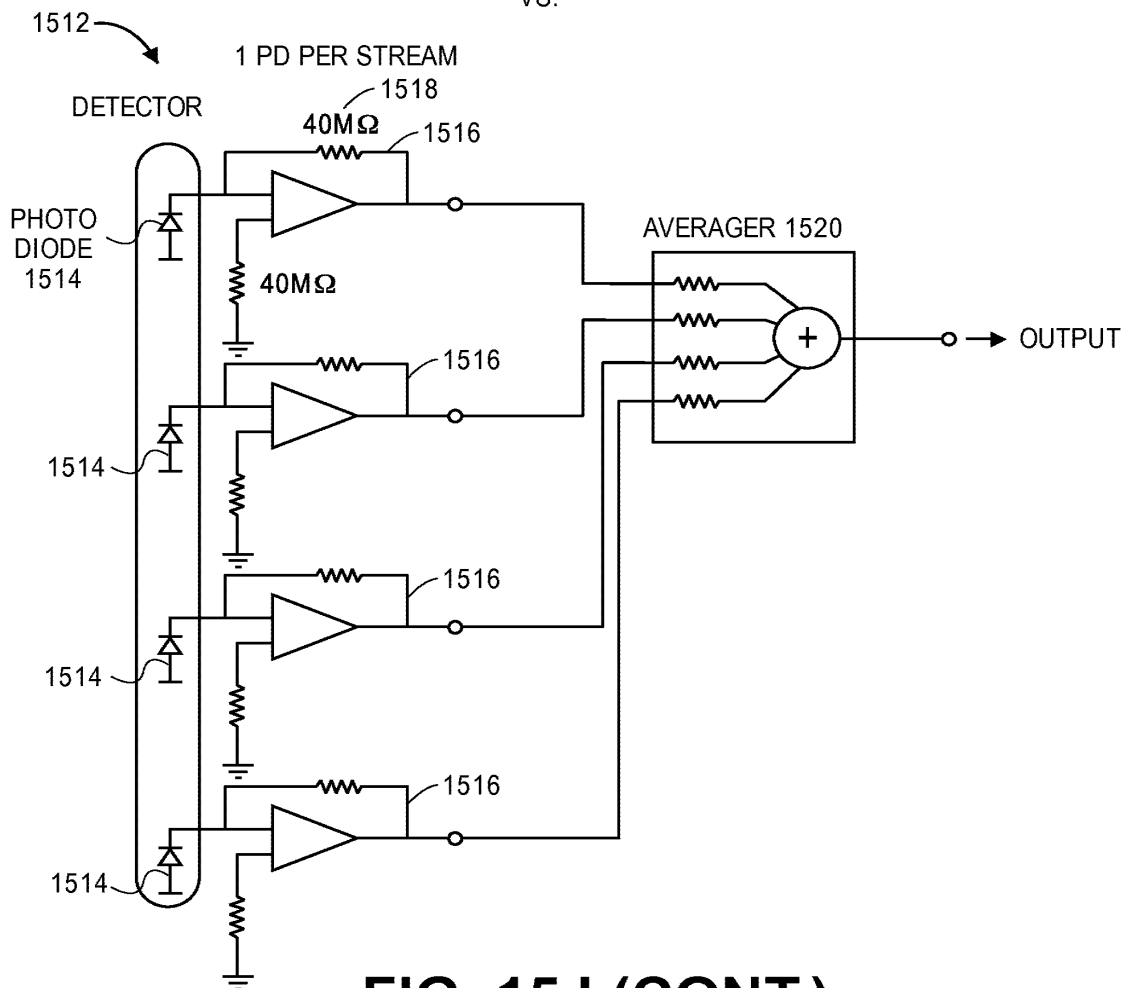
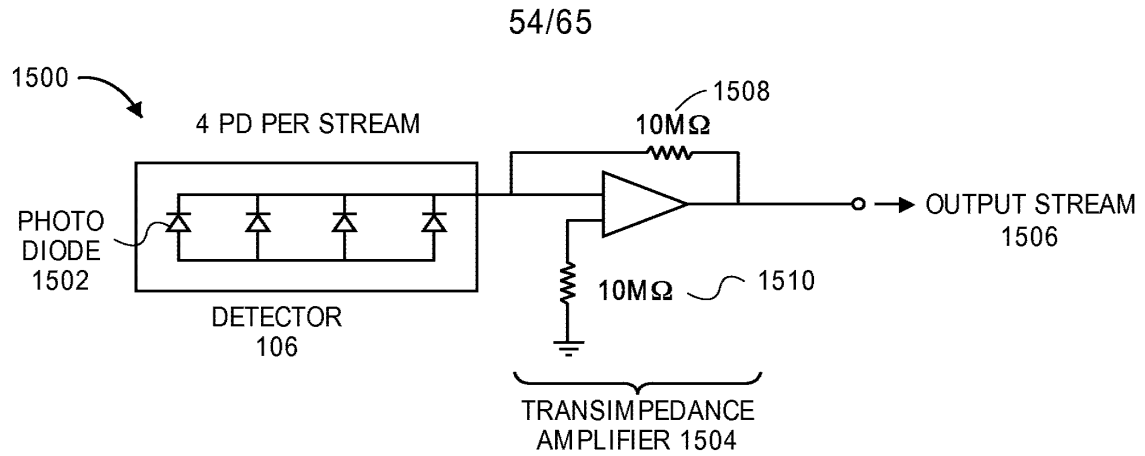


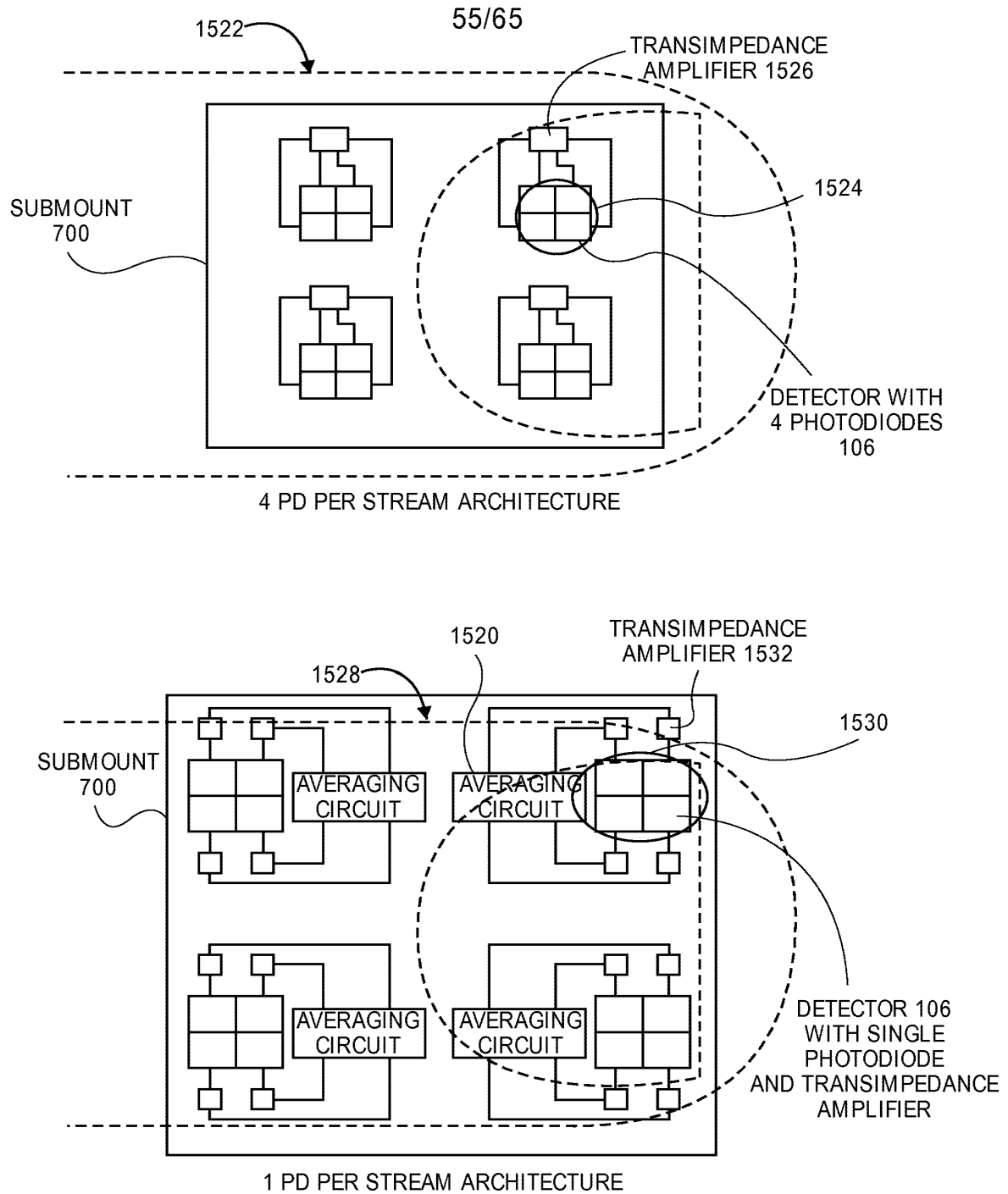
FIG. 151

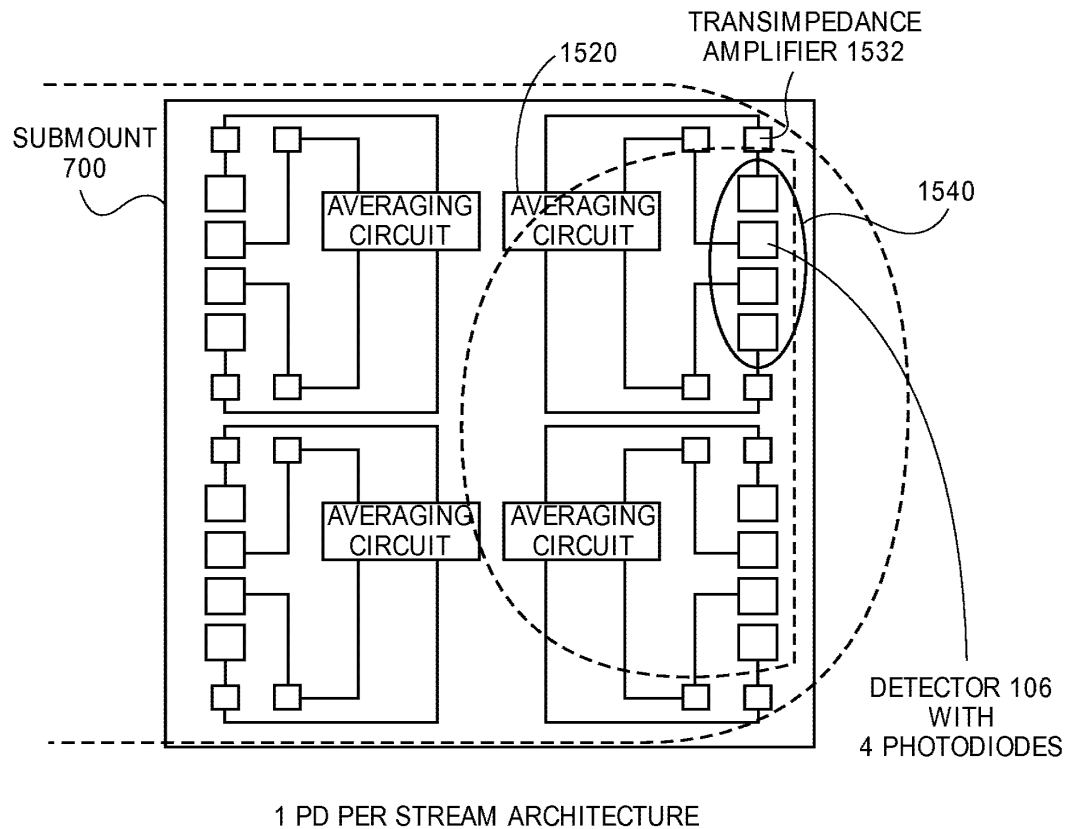
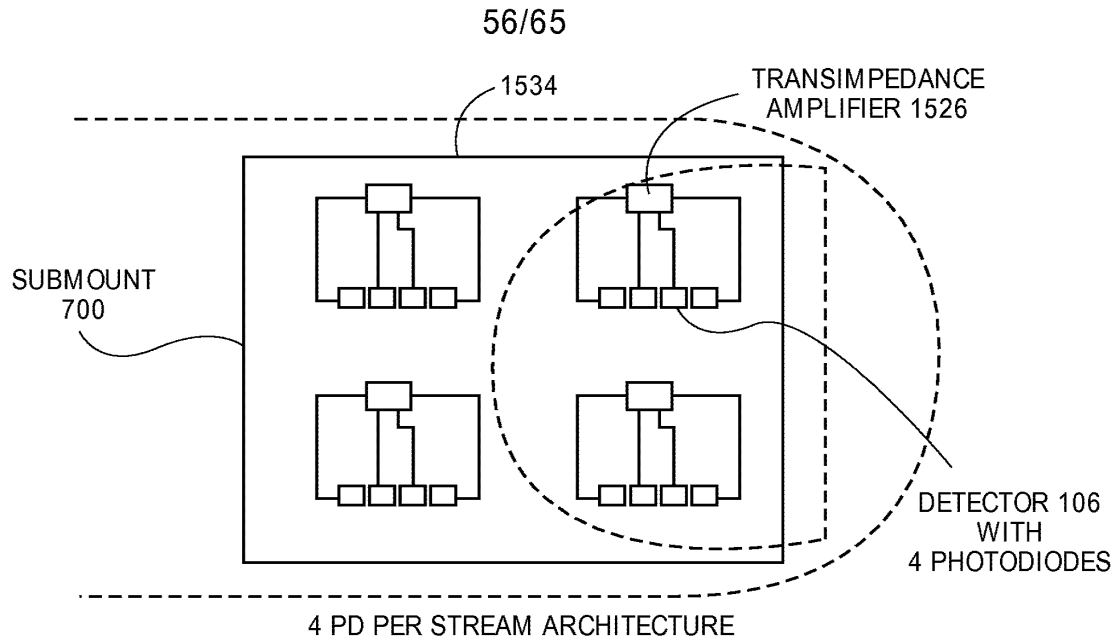
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**FIG. 15J**



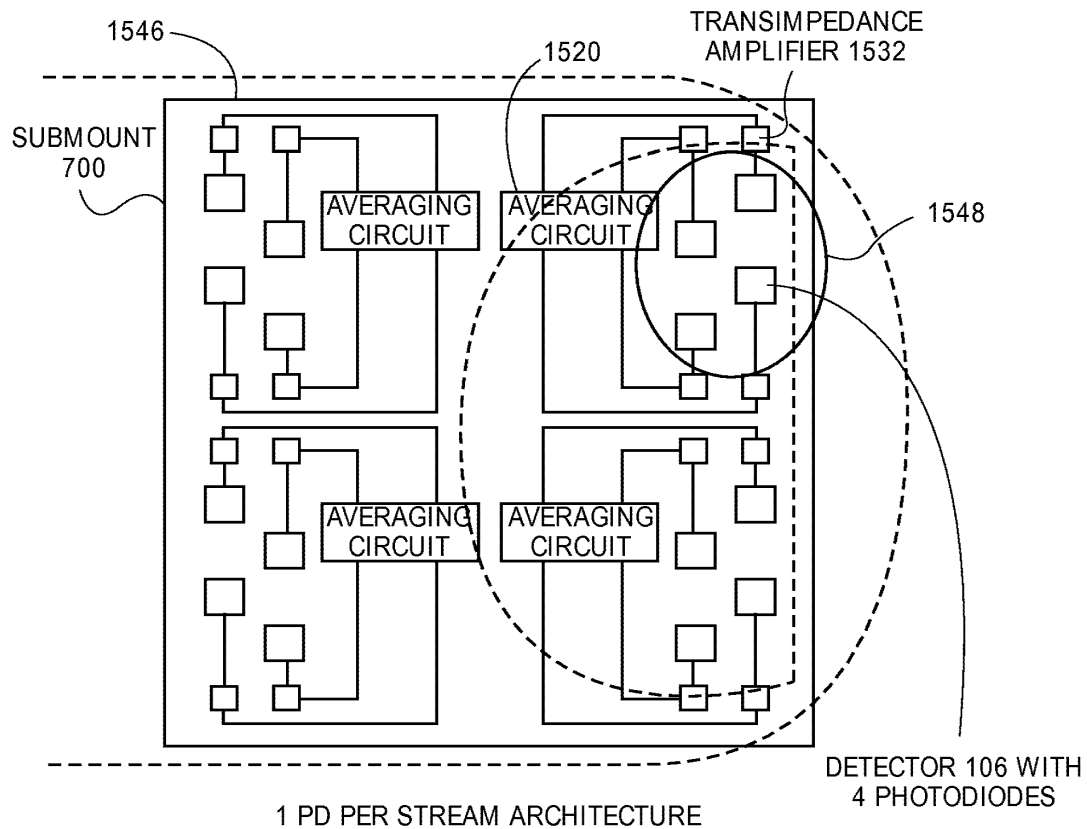
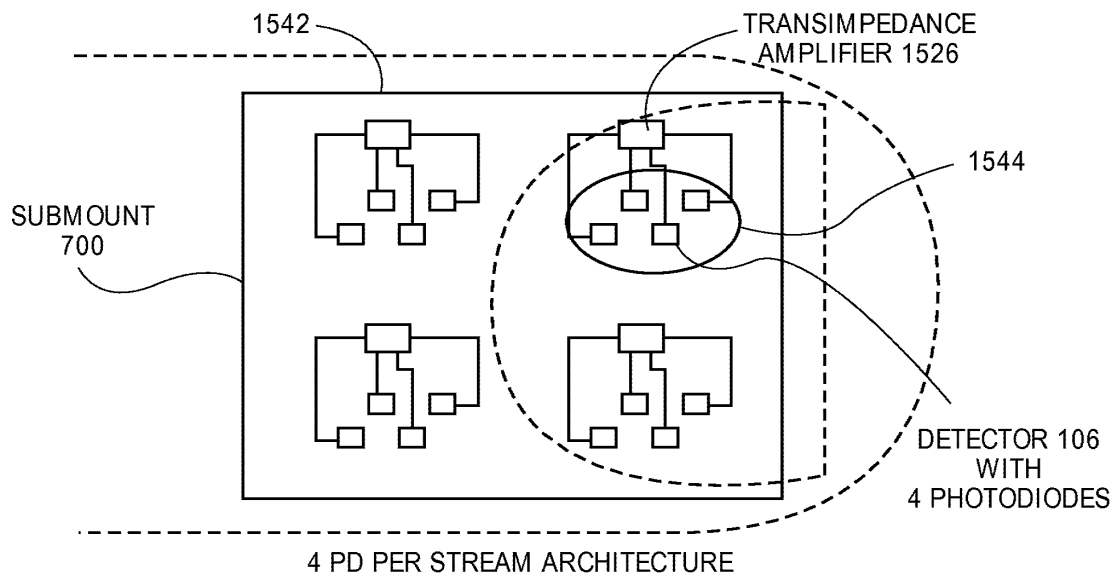


**FIG. 15K**

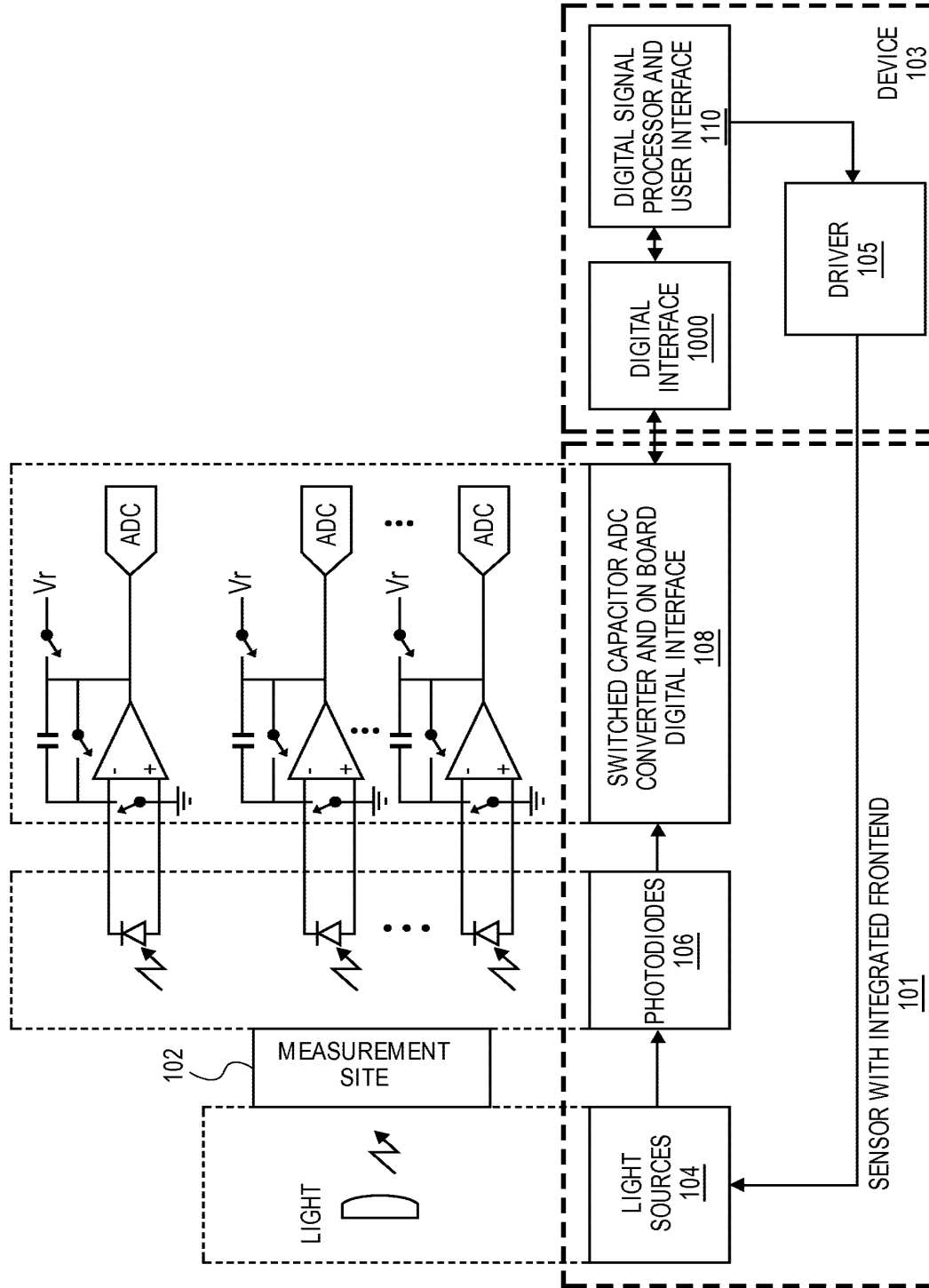


**FIG. 15K (CONT.)**

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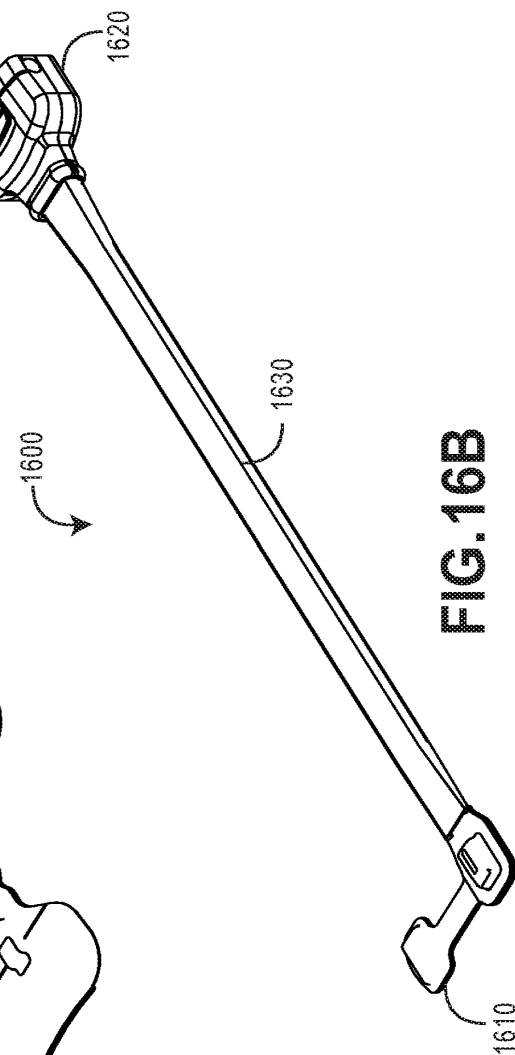
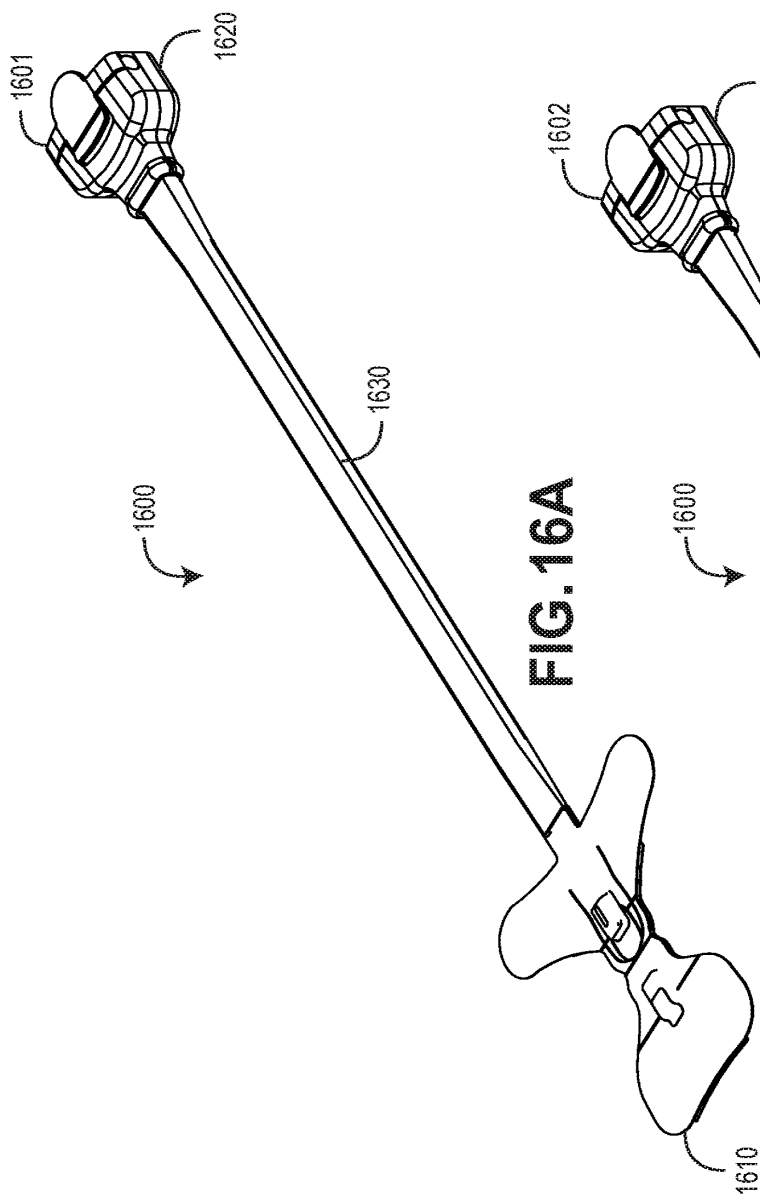
**FIG. 15K (CONT.)**

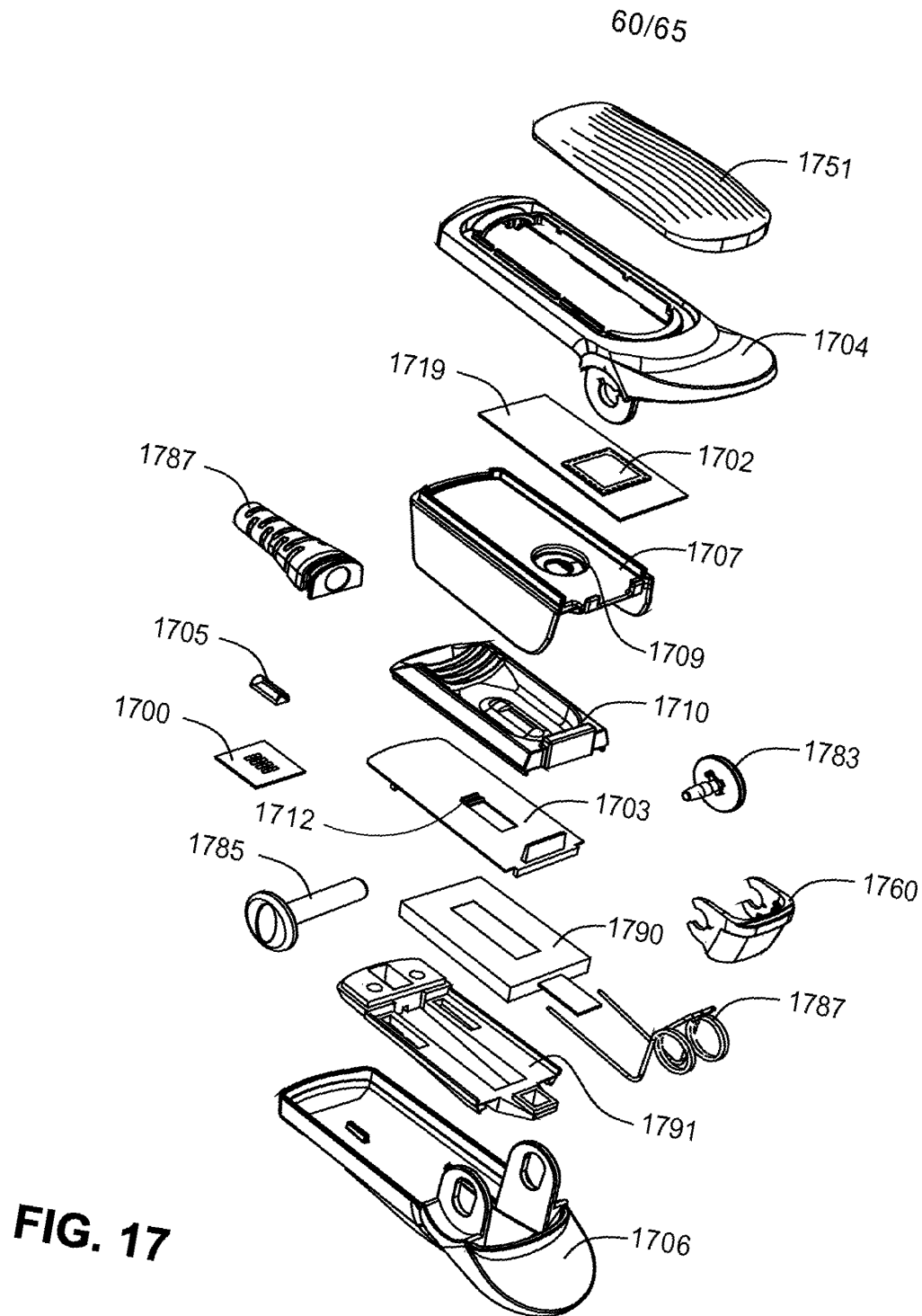
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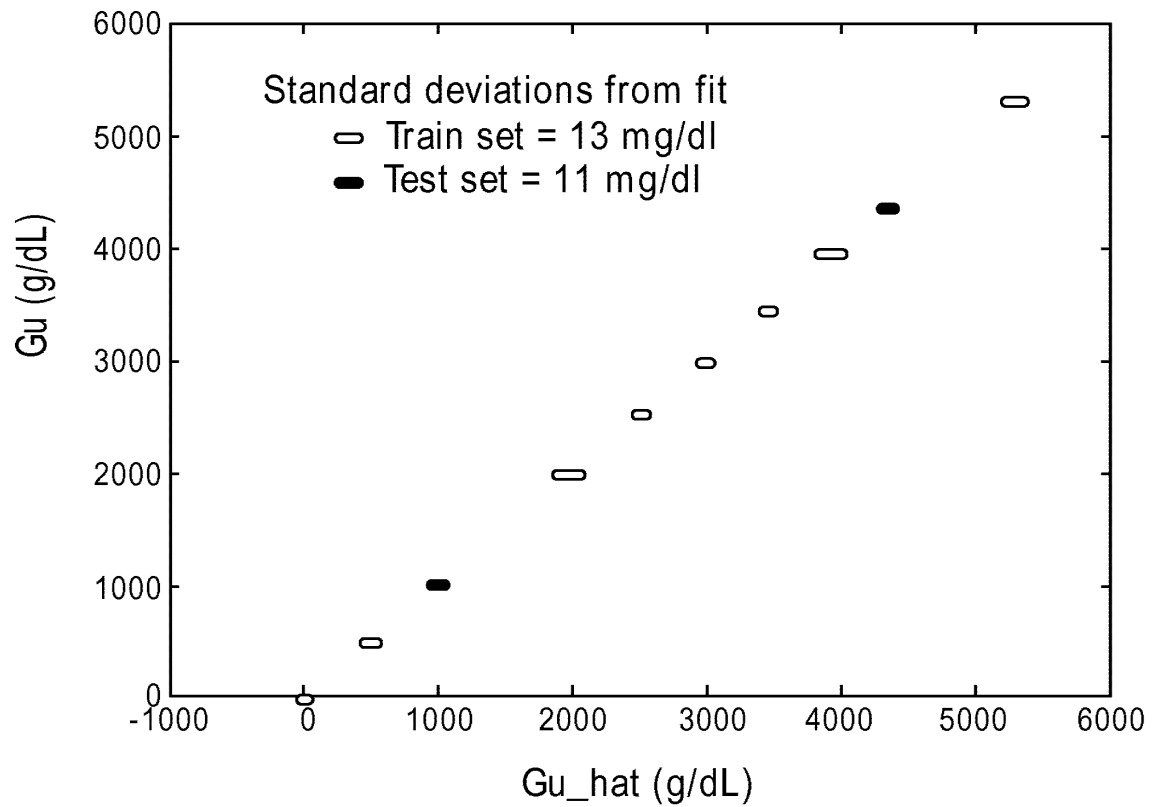
**FIG. 15L**

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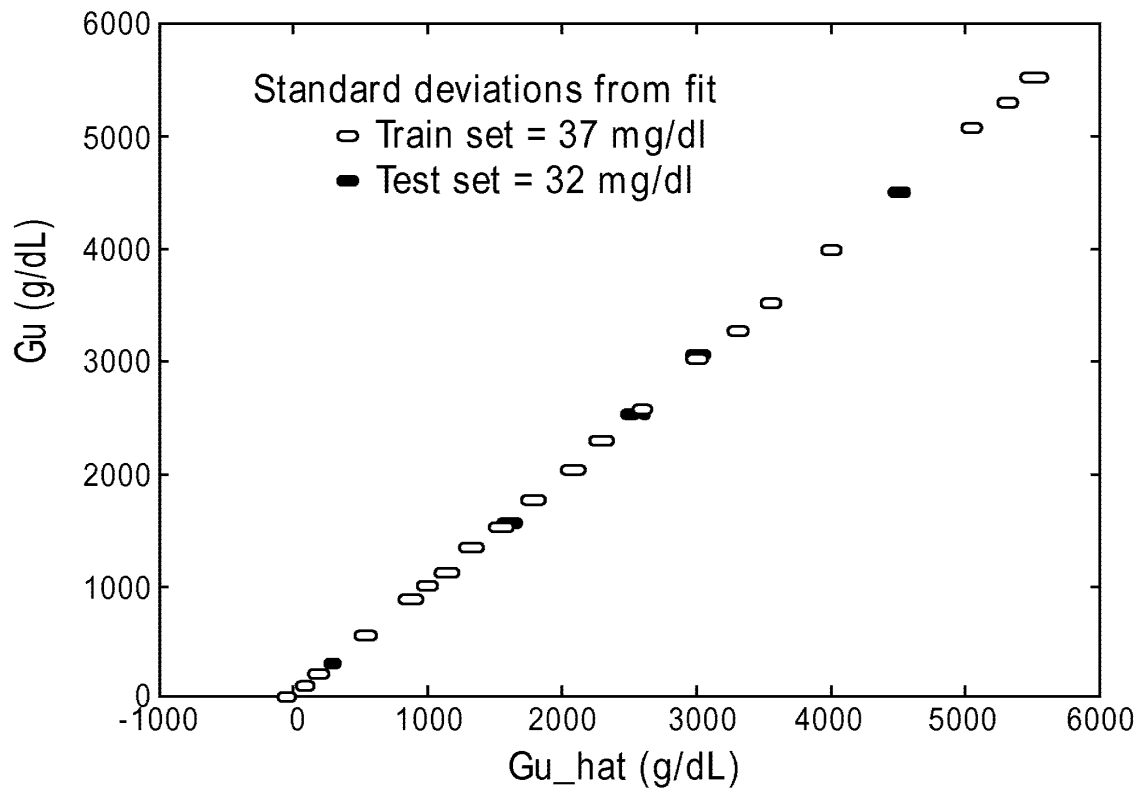


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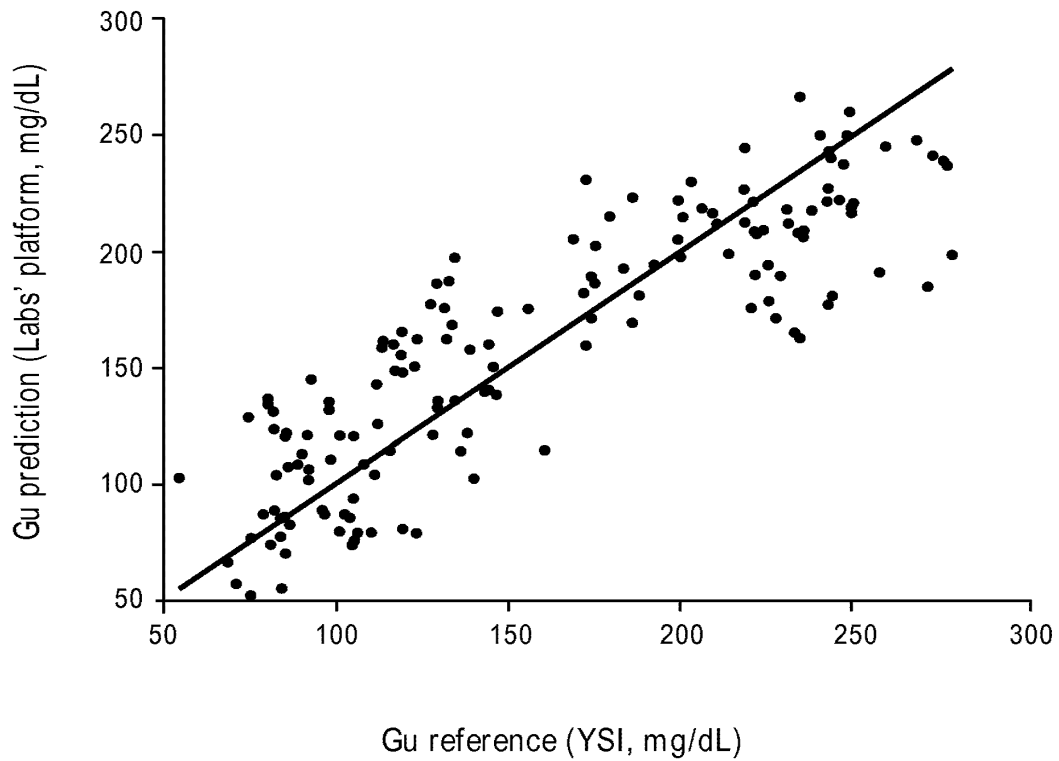
**FIG. 18**



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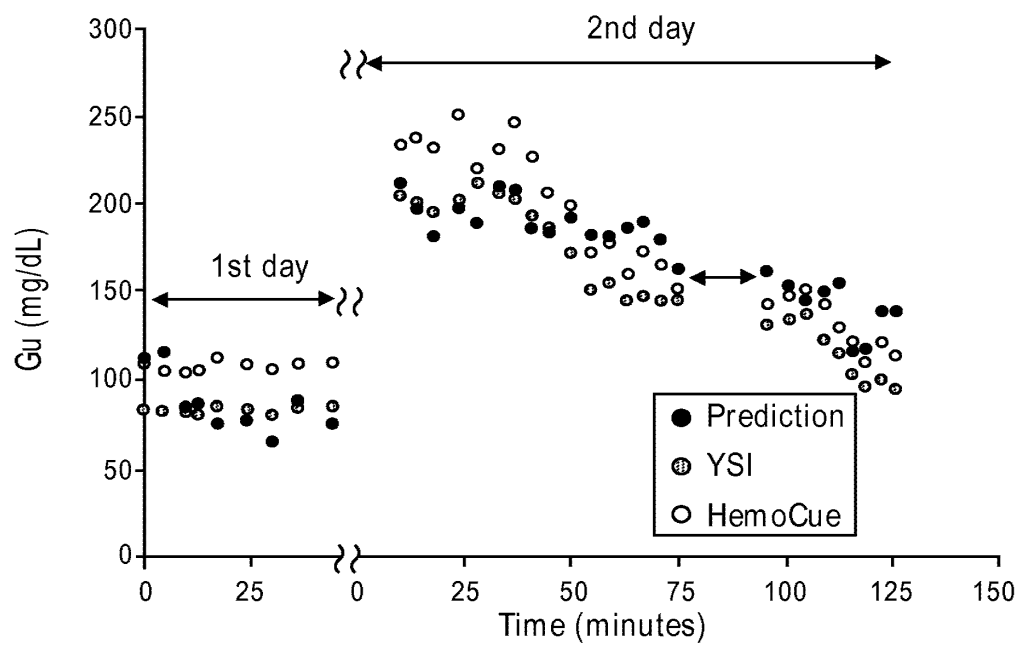
**FIG. 19**

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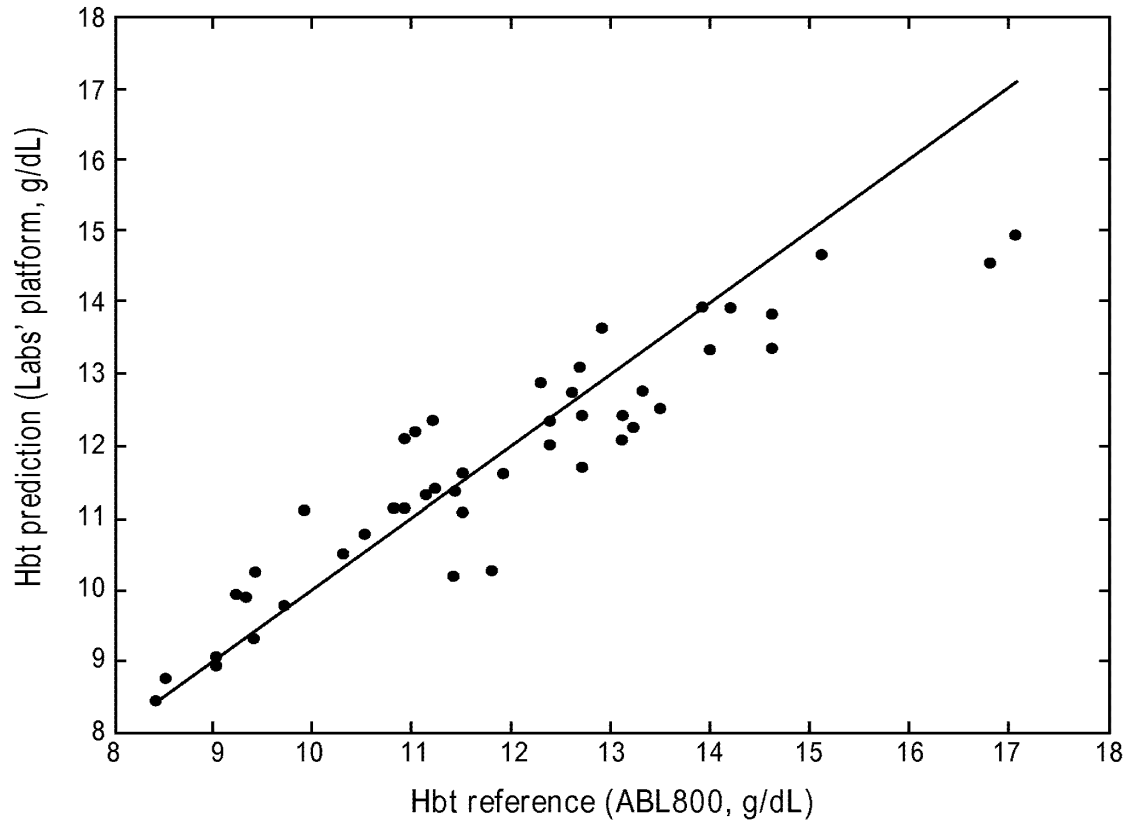


**FIG. 20**

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**FIG. 21**

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**FIG. 22**

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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	MLHUM.002A
		Application Number	
Title of Invention	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS		
<p>The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.</p> <p>This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.</p>			

**Secrecy Order 37 CFR 5.2**

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

**Applicant Information:**

<b>Applicant 1</b>					
<b>Applicant Authority</b>		<input checked="" type="radio"/> Inventor		<input type="radio"/> Legal Representative under 35 U.S.C. 117	
				<input type="radio"/> Party of Interest under 35 U.S.C. 118	
<b>Prefix</b>	<b>Given Name</b>	<b>Middle Name</b>	<b>Family Name</b>	<b>Suffix</b>	
	Massi	Joe E.	Kiani		
<b>Residence Information (Select One)</b> <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
<b>City</b>	Laguna Niguel	<b>State/Province</b>	CA	<b>Country of Residence</b>	US
<b>Citizenship under 37 CFR 1.41(b)</b>		US			
<b>Mailing Address of Applicant:</b>					
<b>Address 1</b>		35 Brindisi			
<b>Address 2</b>					
<b>City</b>	Laguna Niguel	<b>State/Province</b>	CA		
<b>Postal Code</b>	92677	<b>Country</b>	US		
<b>Applicant 2</b>					
<b>Applicant Authority</b>		<input checked="" type="radio"/> Inventor		<input type="radio"/> Legal Representative under 35 U.S.C. 117	
				<input type="radio"/> Party of Interest under 35 U.S.C. 118	
<b>Prefix</b>	<b>Given Name</b>	<b>Middle Name</b>	<b>Family Name</b>	<b>Suffix</b>	
	Marcelo		Lamego		
<b>Residence Information (Select One)</b> <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
<b>City</b>	Coto De Caza	<b>State/Province</b>	CA	<b>Country of Residence</b>	US
<b>Citizenship under 37 CFR 1.41(b)</b>		BR			
<b>Mailing Address of Applicant:</b>					
<b>Address 1</b>		18 Lyra Way			
<b>Address 2</b>					
<b>City</b>	Coto De Caza	<b>State/Province</b>	CA		
<b>Postal Code</b>	92679	<b>Country</b>	US		
<b>Applicant 3</b>					
<b>Applicant Authority</b>		<input checked="" type="radio"/> Inventor		<input type="radio"/> Legal Representative under 35 U.S.C. 117	
				<input type="radio"/> Party of Interest under 35 U.S.C. 118	
<b>Prefix</b>	<b>Given Name</b>	<b>Middle Name</b>	<b>Family Name</b>	<b>Suffix</b>	
	Sean		Merritt		
<b>Residence Information (Select One)</b> <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
<b>City</b>	Lake Forest	<b>State/Province</b>	CA	<b>Country of Residence</b>	US

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<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number		MLHUM.002A	
		Application Number			
Title of Invention		MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			

Citizenship under 37 CFR 1.41(b)		US			
Mailing Address of Applicant:					
Address 1		22273 Vista Verde Drive			
Address 2					
City	Lake Forest	State/Province		CA	
Postal Code	92630	Country	US		

Applicant 4					
Applicant Authority		<input checked="" type="radio"/> Inventor		<input type="radio"/> Legal Representative under 35 U.S.C. 117	
				<input type="radio"/> Party of Interest under 35 U.S.C. 118	
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Cristiano		Dalvi		
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
City	Mission Viejo	State/Province	CA	Country of Residence	US
Citizenship under 37 CFR 1.41(b)		BR			
Mailing Address of Applicant:					
Address 1		21622 Marguerite Pkwy #6			
Address 2					
City	Mission Viejo	State/Province		CA	
Postal Code	92692	Country	US		

Applicant 5					
Applicant Authority		<input checked="" type="radio"/> Inventor		<input type="radio"/> Legal Representative under 35 U.S.C. 117	
				<input type="radio"/> Party of Interest under 35 U.S.C. 118	
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Hung		Vo		
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
City	Garden Grove	State/Province	CA	Country of Residence	US
Citizenship under 37 CFR 1.41(b)		US			
Mailing Address of Applicant:					
Address 1		8801 Mays Ave.			
Address 2					
City	Garden Grove	State/Province		CA	
Postal Code	92844	Country	US		

Applicant 6					
Applicant Authority		<input checked="" type="radio"/> Inventor		<input type="radio"/> Legal Representative under 35 U.S.C. 117	
				<input type="radio"/> Party of Interest under 35 U.S.C. 118	
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Johannes		Bruinsma		
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
City	Mission Viejo	State/Province	CA	Country of Residence	US
Citizenship under 37 CFR 1.41(b)		NL			

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<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number		MLHUM.002A	
		Application Number			
Title of Invention		MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
<b>Mailing Address of Applicant:</b>					
Address 1		27141 Valia			
Address 2					
City	Mission Viejo		State/Province	CA	
Postal Code	92691		Country	US	
<b>Applicant 7</b>					
Applicant Authority		<input checked="" type="radio"/> Inventor		<input type="radio"/> Legal Representative under 35 U.S.C. 117	
				<input type="radio"/> Party of Interest under 35 U.S.C. 118	
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Jeroen		Poeze		
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
City	Mission Viejo		State/Province	CA	Country of Residence
					US
Citizenship under 37 CFR 1.41(b)		NL			
<b>Mailing Address of Applicant:</b>					
Address 1		21622 Marguirite Parkway #342			
Address 2					
City	Mission Viejo		State/Province	CA	
Postal Code	92692		Country	US	
<b>Applicant 8</b>					
Applicant Authority		<input checked="" type="radio"/> Inventor		<input type="radio"/> Legal Representative under 35 U.S.C. 117	
				<input type="radio"/> Party of Interest under 35 U.S.C. 118	
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Ferdyan		Lesmana		
Residence Information (Select One) <input checked="" type="radio"/> US Residency <input type="radio"/> Non US Residency <input type="radio"/> Active US Military Service					
City	Irvine		State/Province	CA	Country of Residence
					US
Citizenship under 37 CFR 1.41(b)		ID			
<b>Mailing Address of Applicant:</b>					
Address 1		42 New Season			
Address 2					
City	Irvine		State/Province	CA	
Postal Code	92602		Country	US	
All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button.					
<input type="button" value="Add"/>					

**Correspondence Information:**

Enter either Customer Number or complete the Correspondence Information section below.  
For further information see 37 CFR 1.33(a).

☐ An Address is being provided for the correspondence information of this application.

Customer Number 20995

Email Address efilng@kmb.com

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<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	MLHUM.002A
		Application Number	
Title of Invention	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS		

**Application Information:**

Title of the Invention	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS		
Attorney Docket Number	MLHUM.002A	Small Entity Status Claimed	<input type="checkbox"/>
Application Type	Nonprovisional		
Subject Matter	Utility		
Suggested Class (if any)		Sub Class (if any)	
Suggested Technology Center (if any)			
Total Number of Drawing Sheets (if any)	65	Suggested Figure for Publication (if any)	

**Publication Information:**

<input type="checkbox"/>	Request Early Publication (Fee required at time of Request 37 CFR 1.219)
<input type="checkbox"/>	<b>Request Not to Publish.</b> I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application <b>has not and will not</b> be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

**Representative Information:**

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Enter either Customer Number or complete the Representative Name section below. If both sections are completed the Customer Number will be used for the Representative Information during processing.			
Please Select One:	<input checked="" type="radio"/> Customer Number	<input type="radio"/> US Patent Practitioner	<input type="radio"/> Limited Recognition (37 CFR 11.9)
Customer Number	20995		

**Domestic Benefit/National Stage Information:**

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, or 365(c) or indicate National Stage entry from a PCT application. Providing this information in the application data sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78(a)(2) or CFR 1.78(a)(4), and need not otherwise be made part of the specification.			
Prior Application Status	Pending	<a href="#">Remove</a>	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
Unknown	non provisional of	61/086060	2008-08-04
Prior Application Status	Pending	<a href="#">Remove</a>	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
Unknown	non provisional of	61/086108	2008-08-04
Prior Application Status	Pending	<a href="#">Remove</a>	



CX-1621

PTO/SB/14 (07-07)

Approved for use through 06/30/2010. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number	MLHUM.002A
		Application Number	
Title of Invention	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS		
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
Unknown	non provisional of	61/086063	2008-08-04
Prior Application Status	Pending	<input type="button" value="Remove"/>	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
Unknown	non provisional of	61/086057	2008-08-04
Prior Application Status	Pending	<input type="button" value="Remove"/>	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)
Unknown	non provisional of	61/091732	2008-08-25
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the <b>Add</b> button.			

**Foreign Priority Information:**

This section allows for the applicant to claim benefit of foreign priority and to identify any prior foreign application for which priority is not claimed. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55(a).			
<input type="button" value="Remove"/>			
Application Number	Country <sup>1</sup>	Parent Filing Date (YYYY-MM-DD)	Priority Claimed
			<input type="radio"/> Yes <input checked="" type="radio"/> No
Additional Foreign Priority Data may be generated within this form by selecting the <b>Add</b> button.			

**Assignee Information:**

Providing this information in the application data sheet does not substitute for compliance with any requirement of part 3 of Title 37 of the CFR to have an assignment recorded in the Office.				
<b>Assignee 1</b>				
If the Assignee is an Organization check here. <input type="checkbox"/>				
Prefix	Given Name	Middle Name	Family Name	Suffix
<b>Mailing Address Information:</b>				
Address 1				
Address 2				
City		State/Province		
Country <sup>1</sup>		Postal Code		
Phone Number		Fax Number		
Email Address				
Additional Assignee Data may be generated within this form by selecting the <b>Add</b> button.				

**Signature:**

A signature of the applicant or representative is required in accordance with 37 CFR 1.33 and 10.18. Please see 37 CFR 1.4(d) for the form of the signature.
--

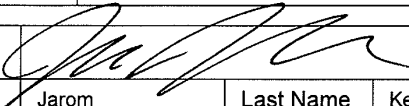
CX-1621

PTO/SB/14 (07-07)

Approved for use through 06/30/2010. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

<b>Application Data Sheet 37 CFR 1.76</b>		Attorney Docket Number		MLHUM.002A	
		Application Number			
Title of Invention		MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
Signature 		Date (YYYY-MM-DD)		2009-08-03	
First Name	Jarom	Last Name	Kesler	Registration Number	57046

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

CX-1621

Filing Date: 08/03/09

PTO/SB/06 (12-04)

Approved for use through 7/31/2006. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Send to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD					Application or Docket Number	
Substitute for Form PTO-875					12/534,827	
<b>APPLICATION AS FILED – PART I</b>						
(Column 1)			(Column 2)		(Column 3)	
FOR	NUMBER FILED	NUMBER EXTRA	SMALL ENTITY		OTHER THAN SMALL ENTITY	
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	RATE (\$)	FEE (\$)	RATE (\$)	FEE (\$)
SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A		N/A	330
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A		N/A	540
TOTAL CLAIMS	34	14			N/A	220
INDEPENDENT CLAIMS (37 CFR 1.16(h))	3	2			x\$52	728
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$270 (\$135 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR		x\$110		x\$220	
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))			195		390	
			TOTAL		TOTAL	2088
* If the difference in column 1 is less than zero, enter "0" in column 2.						
<b>APPLICATION AS AMENDED – PART II</b>						
(Column 1)			(Column 2)		(Column 3)	
AMENDMENT A	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		SMALL ENTITY	
	Total (37 CFR 1.16(i))	Minus	**	=	RATE (\$)	ADDITIONAL FEE (\$)
	Independent (37 CFR 1.16(h))	Minus	***	=	X =	
	Application Size Fee (37 CFR 1.16(s))				X =	
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))				N/A	
			TOTAL		TOTAL	
			ADD'T FEE		ADD'T FEE	
(Column 1) (Column 2) (Column 3)						
AMENDMENT B	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA		SMALL ENTITY	
	Total (37 CFR 1.16(i))	Minus	**	=	RATE (\$)	ADDITIONAL FEE (\$)
	Independent (37 CFR 1.16(h))	Minus	***	=	X =	
	Application Size Fee (37 CFR 1.16(s))				X =	
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))				N/A	
			TOTAL		TOTAL	
			ADD'T FEE		ADD'T FEE	
* If the entry in column 1 is less than the entry in column 2, write "0" in column 3. ** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20". *** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3". The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.						

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Page 614 of 614

Appx58278

UNITED STATES PATENT AND TRADEMARK OFFICE  
**CERTIFICATE OF CORRECTION**

PATENT NO. : 9,277,880 B2  
APPLICATION NO. : 12/829352  
DATED : March 8, 2016  
INVENTOR(S) : Jeroen Poeze et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the Title Page

Item (63), Column 1 at Lines 2-3, Related U.S. Application Data, Change “which is a continuation-in-part of” to --and a continuation-in-part of--.

Item (63), Column 1 at Line 4, Related U.S. Application Data, After “and” insert --a continuation-in-part of application No. 12/497,523, filed on Jul. 2, 2009, now Pat. No. 8,437,825, said application No. 12/497,528 is--.

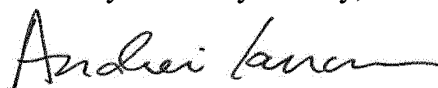
Item (63), Page 2, Column 1 at Lines 5-7, Related U.S. Application Data, Change “which is a continuation-in-part of application No. 12/497,523, filed on Jul. 2, 2009, now Pat. No. 8,437,825” to --said application No. 12/497,523, is a continuation-in-part of application No. 29/323,409, filed on Aug. 25, 2008, now Pat. No. Des. 621,516, and a continuation-in-part of application No. 29/323,408, filed on Aug. 25, 2008, now Pat. No. Des. 606,659--.

In the Specification

In Column 1, Line 15, Change “a continuation of” to --a continuation-in-part of--.

In Column 1, Lines 26-27, Change “a continuation of” to --a continuation-in-part of--.

Signed and Sealed this  
Twenty-first Day of July, 2020



Andrei Iancu  
*Director of the United States Patent and Trademark Office*



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
**United States Patent and Trademark Office**  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/829,352	07/01/2010	Jeroen Poeze	MASCER.002C1	8366

64735	7590	06/29/2020	EXAMINER	
KNOBBE, MARTENS, OLSON & BEAR, LLP			LIU, CHU CHUAN	
MASIMO CORPORATION (MASIMO)				
2040 MAIN STREET				
FOURTEENTH FLOOR				
IRVINE, CA 92614				

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
06/29/2020	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

efiling@knobbe.com  
 jayna.cartee@knobbe.com



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
www.uspto.gov

Patent No.: 9277880  
Issue Date: 03/08/2016  
Appl. No.: 12/829,352  
Filed: 07/01/2010

**PART (A) RESPONSE FOR CERTIFICATES OF CORRECTION**

This is a decision on the Certificate of Correction request filed 15 June 2020.

The request for issuance of Certificate of Correction for the above-identified correction(s) under the provisions of 37 CFR 1.322 and/or 1.323 is hereby:

(Check one)

☒ Approved ☐ Approved in Part ☐ Denied

Comments: \_\_\_\_\_

**PART (B) PETITION UNDER 37 CFR 1.324 OR 37 CFR 1.48**

☐ This is a decision on the petition filed \_\_\_\_\_ to correct inventorship under 37 CFR 1.324.

☐ This is a decision on the request under 37 CFR 1.48, petition filed \_\_\_\_\_. In view of the fact that the patent has already issued, the request under 37 CFR 1.48 has been treated as a petition to correct inventorship under 37 CFR 1.324.

The petition is hereby: ☐ Granted ☐ Dismissed

Comment: \_\_\_\_\_

The patented filed is being forwarded to Certificate of Corrections Branch for issuance of a certificate naming only the actual inventor or inventors.

/TSE W CHEN/  
Supervisory Patent Examiner, Art Unit 3791  
Technology Center 3700  
Phone: (571)272-3672

Certificates of Correction Branch email: CustomerServiceCoC@uspto.gov CoC Central Phone Number: (703) 756-1814



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents  
United States Patent and Trademark Office  
P.O. Box 1450  
Alexandria, VA 22313-1450  
www.uspto.gov

Patent No.: 9277880  
Issue Date: 03/08/2016  
Appl. No.: 12/829,352  
Filed: 07/01/2010

**PART (A) RESPONSE FOR CERTIFICATES OF CORRECTION**

This is a decision on the Certificate of Correction request filed 15 June 2020.

The request for issuance of Certificate of Correction for the above-identified correction(s) under the provisions of 37 CFR 1.322 and/or 1.323 is hereby:

(Check one)

☒ Approved

☐ Approved in Part

☐ Denied

Comments: \_\_\_\_\_

**PART (B) PETITION UNDER 37 CFR 1.324 OR 37 CFR 1.48**

☐ This is a decision on the petition filed \_\_\_\_\_ to correct inventorship under 37 CFR 1.324.

☐ This is a decision on the request under 37 CFR 1.48, petition filed \_\_\_\_\_. In view of the fact that the patent has already issued, the request under 37 CFR 1.48 has been treated as a petition to correct inventorship under 37 CFR 1.324.

The petition is hereby:

☐ Granted

☐ Dismissed

Comment: \_\_\_\_\_

The patented filed is being forwarded to Certificate of Corrections Branch for issuance of a certificate naming only the actual inventor or inventors.

/TSE W CHEN/

Supervisory Patent Examiner, Art Unit 3791

Technology Center 3700

Phone: (571)272-3672

Certificates of Correction Branch email: CustomerServiceCoC@uspto.gov CoC Central Phone Number: (703) 756-1814

Docket No.: MAS CER.002C1

Page 1 of 1

**REQUEST FOR CERTIFICATE OF CORRECTION**

First Inventor	:	Jeroen Poeze
App. No.	:	12/829352
Filed	:	July 1, 2010
Patent No.	:	9,277,880
Issue Date	:	March 8, 2016
Title	:	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
Conf. No.	:	8366

Commissioner for Patents  
Office of Data Management  
**Attention:** Certificates of Correction Branch  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Commissioner:

Enclosed for filing is a Certificate of Correction in connection with the above-identified patent.

The Certificate of Correction includes a request to correct typographical errors in the domestic priority application data as printed on the patent grant. The correct domestic priority claim is evidenced by the filing receipt in this application dated October 7, 2015, a copy of which is provided with this request.

Some of the errors cited in the Certificate of Correction appear to have been incurred through the fault of the PTO (see 35 USC § 254, 37 CFR § 1.322, and MPEP § 1480). However, because this may not apply to each item in the Certificate of Correction, the \$150 fee under 37 CFR § 1.20(a) is submitted herewith. Please charge any additional fees to our Deposit Account No. 11 1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: June 15, 2020

By: /Scott Cromar/ \_\_\_\_\_  
Scott A. Cromar  
Registration No. 65,066  
Registered Practitioner  
(949) 760-0404



**UNITED STATES PATENT AND TRADEMARK OFFICE  
CERTIFICATE OF CORRECTION**

**PATENT NO.** : 9,277,880

Page 1 of 1

**APPLICATION NO.** : 12/829352

**ISSUE DATE** : March 8, 2016

**INVENTOR(S)** : Jeroen Poeze

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the Title Page:

Item No. (63), Page 1, Column 1 at Lines 2-3, Related U.S. Application Data, Change “which is a continuation-in-part of” to --and a continuation-in-part of--.

Item No. (63), Page 1, Column 1 at Line 4, Related U.S. Application Data, After “and” insert --a continuation-in-part of application No. 12/497,523 , filed on Jul. 2, 2009, now Pat. No. 8,437,825, said application No. 12/497,528 is--.

Item No. (63), Page 2, Column 1 at Lines 5-7, Related U.S. Application Data, Change “which is a continuation-in-part of application No. 12/497,523, filed on Jul. 2, 2009, now Pat. No. 8,437,825” to --said application No. 12/497,523, is a continuation-in-part of application No. 29/323,409, filed on Aug. 25, 2008, now Pat. No. Des. 621,516, and a continuation-in-part of application No. 29/323,408, filed on Aug. 25, 2008, now Pat. No. Des. 606,659--.

In the Specification:

In Column 1, Line 15, Change “a continuation of” to --a continuation-in-part of--.

In Column 1, Lines 26-27, Change “a continuation of” to --a continuation-in-part of--.

**MAILING ADDRESS OF SENDER:**

Scott A. Cromar  
KNOBBE, MARTENS, OLSON & BEAR, LLP  
2040 Main Street, 14<sup>th</sup> Floor  
Irvine, California 92614

DOCKET NO. MASCER.002C1



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
12/829,352	07/01/2010	3777	1594	CERCA.002C1	22	3

CONFIRMATION NO. 8366

## CORRECTED FILING RECEIPT

20995

KNOBBE MARTENS OLSON & BEAR LLP  
 2040 MAIN STREET  
 FOURTEENTH FLOOR  
 IRVINE, CA 92614



CC00000077884891

Date Mailed: 10/07/2015

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

## Inventor(s)

Jeroen Poeze, Mission Viejo, CA;  
 Marcelo Lamego, Coto De Caza, CA;  
 Sean Merritt, Lake Forest, CA;  
 Cristiano Dalvi, Mission Viejo, CA;  
 Hung Vo, Garden Grove, CA;  
 Johannes Bruinsma, Mission Viejo, CA;  
 Ferdyan Lesmana, Irvine, CA;  
 Massi Joe E. Kiani, Laguna Niguel, CA;

## Applicant(s)

Jeroen Poeze, Mission Viejo, CA;  
 Marcelo Lamego, Coto De Caza, CA;  
 Sean Merritt, Lake Forest, CA;  
 Cristiano Dalvi, Mission Viejo, CA;  
 Hung Vo, Garden Grove, CA;  
 Johannes Bruinsma, Mission Viejo, CA;  
 Ferdyan Lesmana, Irvine, CA;  
 Massi Joe E. Kiani, Laguna Niguel, CA;

**Power of Attorney:** The patent practitioners associated with Customer Number 20995

**Domestic Priority data as claimed by applicant**

This application is a CON of 12/534,827 08/03/2009 ABN  
 which claims benefit of 61/086,060 08/04/2008  
 and claims benefit of 61/086,108 08/04/2008  
 and claims benefit of 61/086,063 08/04/2008  
 and claims benefit of 61/086,057 08/04/2008

page 1 of 4

and claims benefit of 61/091,732 08/25/2008  
 This application 12/829,352  
 is a CIP of 12/497,528 07/02/2009 PAT 8577431  
 which claims benefit of 61/086,060 08/04/2008  
 and claims benefit of 61/086,108 08/04/2008  
 and claims benefit of 61/086,063 08/04/2008  
 and claims benefit of 61/086,057 08/04/2008  
 and claims benefit of 61/078,228 07/03/2008  
 and claims benefit of 61/078,207 07/03/2008  
 and claims benefit of 61/091,732 08/25/2008  
 and is a CIP of 29/323,409 08/25/2008 PAT D621516  
 and is a CIP of 29/323,408 08/25/2008 PAT D606659  
 This application 12/829,352  
 is a CIP of 12/497,523 07/02/2009 PAT 8437825  
 which claims benefit of 61/086,060 08/04/2008  
 and claims benefit of 61/086,108 08/04/2008  
 and claims benefit of 61/086,063 08/04/2008  
 and claims benefit of 61/086,057 08/04/2008  
 and claims benefit of 61/078,228 07/03/2008  
 and claims benefit of 61/078,207 07/03/2008  
 and claims benefit of 61/091,732 08/25/2008  
 and is a CIP of 29/323,409 08/25/2008 PAT D621516  
 and is a CIP of 29/323,408 08/25/2008 PAT D606659

**Foreign Applications** for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see <http://www.uspto.gov> for more information.) - None.

*Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.*

**If Required, Foreign Filing License Granted:** 07/16/2010

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 12/829,352**

**Projected Publication Date:** Not Applicable

**Non-Publication Request:** No

**Early Publication Request:** No

**Title**

MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS

**Preliminary Class**

600

**Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications:**

## **PROTECTING YOUR INVENTION OUTSIDE THE UNITED STATES**

Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international

page 2 of 4

application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at <http://www.uspto.gov/web/offices/pac/doc/general/index.html>.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, <http://www.stopfakes.gov>. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

## **LICENSE FOR FOREIGN FILING UNDER**

### **Title 35, United States Code, Section 184**

### **Title 37, Code of Federal Regulations, 5.11 & 5.15**

#### **GRANTED**

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless an earlier license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been granted under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date thereof unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and the national

security or the export of technical data. Licensees should apprise themselves of current regulations especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Bureau of Industry and Security, Department of Commerce (15 CFR parts 730-774); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

**NOT GRANTED**

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12, if a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a secrecy order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

---

***SelectUSA***

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The U.S. offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to promote and facilitate business investment. SelectUSA provides information assistance to the international investor community; serves as an ombudsman for existing and potential investors; advocates on behalf of U.S. cities, states, and regions competing for global investment; and counsels U.S. economic development organizations on investment attraction best practices. To learn more about why the United States is the best country in the world to develop technology, manufacture products, deliver services, and grow your business, visit <http://www.SelectUSA.gov> or call +1-202-482-6800.

Electronic Patent Application Fee Transmittal				
<b>Application Number:</b>	12829352			
<b>Filing Date:</b>	01-Jul-2010			
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS			
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze			
<b>Filer:</b>	Scott Cromar/Frances Tsai			
<b>Attorney Docket Number:</b>	MASCER.002C1			
Filed as Large Entity				
<b>Filing Fees for Utility under 35 USC 111(a)</b>				
<b>Description</b>	<b>Fee Code</b>	<b>Quantity</b>	<b>Amount</b>	<b>Sub-Total in USD(\$)</b>
<b>Basic Filing:</b>				
<b>Pages:</b>				
<b>Claims:</b>				
<b>Miscellaneous-Filing:</b>				
<b>Petition:</b>				
<b>Patent-Appeals-and-Interference:</b>				
<b>Post-Allowance-and-Post-Issuance:</b>				
CERTIFICATE OF CORRECTION	1811	1	150	150

CX-1622

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				150

CX-1622

<b>Electronic Acknowledgement Receipt</b>	
<b>EFS ID:</b>	39717872
<b>Application Number:</b>	12829352
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	8366
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	64735
<b>Filer:</b>	Scott Cromar/Wendy Castorena
<b>Filer Authorized By:</b>	Scott Cromar
<b>Attorney Docket Number:</b>	MASCER.002C1
<b>Receipt Date:</b>	15-JUN-2020
<b>Filing Date:</b>	01-JUL-2010
<b>Time Stamp:</b>	14:38:45
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	\$150
RAM confirmation Number	E20206EE40313809
Deposit Account	111410
Authorized User	Wendy Castorena
<p>The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:</p> <p>37 CFR 1.17 (Patent application and reexamination processing fees)</p> <p>37 CFR 1.16 (National application filing, search, and examination fees)</p>	

Page 13 of 1082

**Appx58291**



CX-1622

**File Listing:**

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Certificate of Correction	CoC_C1.pdf	228590	no	6
			0ad9906d019987c4539f263affcae770a4251f6e		

**Warnings:****Information:**

2	Fee Worksheet (SB06)	fee-info.pdf	30191	no	2
			45a41293932163bc9d4c49ba3cacc9b7f1b734de		

**Warnings:****Information:**

<b>Total Files Size (in bytes):</b>	258781
-------------------------------------	--------

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

**New Applications Under 35 U.S.C. 111**

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

**National Stage of an International Application under 35 U.S.C. 371**

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

**New International Application Filed with the USPTO as a Receiving Office**

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NUMBER	PATENT NUMBER	GROUP ART UNIT	REQUEST ID
12/829,352	9277880	3777	41932

**PAIR Correspondence Address/Fee Address Change**

The following fields have been changed to Customer Number 64735 on 06/19/2017 via Private PAIR in view of the certification copied below that authorized the change.

- Correspondence Address

The address for Customer Number 64735 is:

64735

KNOBBE, MARTENS, OLSON & BEAR, LLP

MASIMO CORPORATION (MASIMO)

2040 MAIN STREET

FOURTEENTH FLOOR

IRVINE, CA 92614

**I certify, in accordance with 37 CFR 1.4(d)(4) that I am:**

An attorney or Agent of Record registered to practice before the Patent and Trademark Office who has been given power of attorney in this application

<b>Signature:</b>	/Jarom Kesler/
<b>Name:</b>	Jarom Kesler
<b>Registration Number:</b>	57046



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
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APPLICATION NUMBER	PATENT NUMBER	GROUP ART UNIT	REQUEST ID
12/829,352	9277880	3777	41932

**PAIR Correspondence Address/Fee Address Change**

The following fields have been changed to Customer Number 64735 on 06/19/2017 via Private PAIR in view of the certification copied below that authorized the change.

- Maintenance Fee Address

The address for Customer Number 64735 is:

64735

KNOBBE, MARTENS, OLSON & BEAR, LLP

MASIMO CORPORATION (MASIMO)

2040 MAIN STREET

FOURTEENTH FLOOR

IRVINE, CA 92614

**I certify, in accordance with 37 CFR 1.4(d)(4) that I am:**

An attorney or Agent of Record registered to practice before the Patent and Trademark Office who has been given power of attorney in this application

<b>Signature:</b>	/Jarom Kesler/
<b>Name:</b>	Jarom Kesler
<b>Registration Number:</b>	57046



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
12/829,352	07/01/2010	Jeroen Poeze	MASCER.002C1

CONFIRMATION NO. 8366

## POWER OF ATTORNEY NOTICE

20995

KNOBBE MARTENS OLSON & BEAR LLP  
 2040 MAIN STREET  
 FOURTEENTH FLOOR  
 IRVINE, CA 92614



\*OC000000091376817\*

Date Mailed: 05/16/2017

## NOTICE REGARDING CHANGE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 05/10/2017.

- The Power of Attorney to you in this application has been revoked by the assignee who has intervened as provided by 37 CFR 3.71. Future correspondence will be mailed to the new address of record(37 CFR 1.33).

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at (571) 272-4000 or (571) 272-4200 or 1-888-786-0101.

/sleutchit/



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
12/829,352	07/01/2010	Jeroen Poeze	MASCER.002C1

CONFIRMATION NO. 8366

## POA ACCEPTANCE LETTER

64735

KNOBBE, MARTENS, OLSON & BEAR, LLP  
 MASIMO CORPORATION (MASIMO)  
 2040 MAIN STREET  
 FOURTEENTH FLOOR  
 IRVINE, CA 92614



\*OC000000091377049\*

Date Mailed: 05/16/2017

## NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 05/10/2017.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at (571) 272-4000 or (571) 272-4200 or 1-888-786-0101.

/sleutchit/

Docket No.: MASIMO.000GEN

Customer No. 64,735

**REVOCATION  
AND  
GENERAL POWER OF ATTORNEY**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

The undersigned is an empowered representative of the Assignee and hereby appoints the registrants of Knobbe, Martens, Olson & Bear, LLP, **Customer No. 64,735**, as attorneys and agents to represent the Assignee before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned to the Assignee according to the USPTO assignment records or assignment documents supplied with an accompanying Statement Under 37 CFR § 3.73(b). This appointment is to be to the exclusion of the inventor(s) and his attorney(s) in accordance with the provisions of 37 CFR § 3.71.

All previous powers of attorney for the below named Assignee are hereby revoked.

A Statement Under 37 CFR § 3.73(b), signed by a registrant of Knobbe, Martens, Olson & Bear, LLP, is attached setting forth a full chain of title for the subject application owned by the Assignee named below.

Please recognize or change the correspondence address for the above-identified application to **Customer No. 64,735**.

By:



Date:

8/1/2011

Name: Thomas McClenahan

Assignee: MASIMO CORPORATION

Address: 40 Parker, Irvine, CA 92618

Title: Vice President and Assistant General Counsel

11676102  
080111

CX-1622

Electronic Acknowledgement Receipt	
<b>EFS ID:</b>	29170787
<b>Application Number:</b>	12829352
<b>International Application Number:</b>	
<b>Confirmation Number:</b>	8366
<b>Title of Invention:</b>	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
<b>First Named Inventor/Applicant Name:</b>	Jeroen Poeze
<b>Customer Number:</b>	20995
<b>Filer:</b>	Jarom D. Kesler/ThuyQuyen Nguyen
<b>Filer Authorized By:</b>	Jarom D. Kesler
<b>Attorney Docket Number:</b>	MASCER.002C1
<b>Receipt Date:</b>	10-MAY-2017
<b>Filing Date:</b>	01-JUL-2010
<b>Time Stamp:</b>	14:34:29
<b>Application Type:</b>	Utility under 35 USC 111(a)

**Payment information:**

Submitted with Payment	no
------------------------	----

**File Listing:**

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Assignee showing of ownership per 37 CFR 3.73	MASCER_002C1_Stmnt373.pdf	32257 f6e280c1e2c51a516a9770f862c9283f9f53e470	no	2

**Warnings:**

Page 20 of 1082

Appx58298

CX-1622

<b>Information:</b>					
2	Power of Attorney	MASIMO_GENPOA_PreAIA.pdf	50520	no	1
			277a9166011fdf5b6853e2ad5c621b417e522fab		
<b>Warnings:</b>					
<b>Information:</b>					
Total Files Size (in bytes):			82777		
<p>This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.</p> <p><b><u>New Applications Under 35 U.S.C. 111</u></b>  If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.</p> <p><b><u>National Stage of an International Application under 35 U.S.C. 371</u></b>  If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.</p> <p><b><u>New International Application Filed with the USPTO as a Receiving Office</u></b>  If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.</p>					



Docket No.: MAS CER.002C1

Customer No. 64735

**STATEMENT UNDER 37 CFR § 3.73  
ESTABLISHMENT OF ASSIGNEE**

First Inventor	:	Jeroen Poeze
App. No.	:	12/829352
Filed	:	July 1, 2010
For	:	MULTI-STREAM DATA COLLECTION SYSTEM FOR NONINVASIVE MEASUREMENT OF BLOOD CONSTITUENTS
Examiner	:	Liu, Chu Chuan
Group Art Unit	:	3777
Conf No.	:	8366

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

This document is being filed with a copy of a Power of Attorney signed by the Assignee. This Statement sets forth the chain of title of the above-identified application.

Masimo Corporation, a Corporation, is the Assignee of the entire right, title, and interest of the above-referenced application by virtue of:

A chain of title, in reverse order, from the inventor(s) to the current Assignee as shown by the following recorded assignments:

1. Assignment from Cercacor Laboratories, Inc. to Masimo Corporation recorded in the United States Patent and Trademark Office on March 9, 2016, at Reel 038049, and Frame 0074.
2. Assignment from Masimo Laboratories, Inc. to Cercacor Laboratories, Inc. recorded in the United States Patent and Trademark Office on May 18, 2012, at Reel 028236, and Frame 0461.
3. Assignment from Inventors to Masimo Laboratories, Inc. recorded in the United States Patent and Trademark Office on January 8, 2010, at Reel 023757, and Frame 0332.

**Appl. No. : 12/829352**  
**Filed : July 1, 2010**

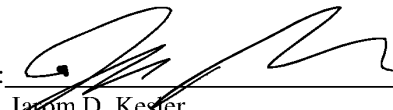
**Docket No. MASCEr.002C1**  
**Customer No. 64735**

The undersigned is an agent of Customer No. 64735 and is authorized to act on behalf of the Assignee. Please recognize or change the correspondence address for the above-identified application to **Customer No. 64735.**

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: May 10, 2017

By:   
Jarom D. Kesler  
Registration No. 57,046  
Attorney of Record  
Customer No. 64735  
(949) 760-0404

25446334



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
 United States Patent and Trademark Office  
 Address: COMMISSIONER FOR PATENTS  
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 Alexandria, Virginia 22313-1450  
 www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/829,352	03/08/2016	9277880	MASCE.002C1	8366

20995 7590 02/17/2016  
 KNOBBE MARTENS OLSON & BEAR LLP  
 2040 MAIN STREET  
 FOURTEENTH FLOOR  
 IRVINE, CA 92614

**ISSUE NOTIFICATION**

The projected patent number and issue date are specified above.

**Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)**  
 (application filed on or after May 29, 2000)

The Patent Term Adjustment is 423 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Data Management (ODM) at (571)-272-4200.

**APPLICANT(s)** (Please see PAIR WEB site <http://pair.uspto.gov> for additional applicants):

Jeroen Poeze, Mission Viejo, CA;  
 Marcelo Lamego, Coto De Caza, CA;  
 Sean Merritt, Lake Forest, CA;  
 Cristiano Dalvi, Mission Viejo, CA;  
 Hung Vo, Garden Grove, CA;  
 Johannes Bruinsma, Mission Viejo, CA;  
 Ferdyan Lesmana, Irvine, CA;  
 Massi Joe E. Kiani, Laguna Niguel, CA;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit [SelectUSA.gov](http://SelectUSA.gov).

<b><i>Examiner-Initiated Interview Summary</i></b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	12/829,352	POEZE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	CHU CHUAN (JJ) LIU	3777	

All participants (applicant, applicant's representative, PTO personnel):

(1) Chu Chuan Liu. (3) \_\_\_\_\_.

(2) Scott Cromar. (4) \_\_\_\_\_.

Date of Interview: 08 February 2016.

Type: ☒ Telephonic ☐ Video Conference  
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☐ No.  
If Yes, brief description: \_\_\_\_\_.

Issues Discussed ☐101 ☐112 ☐102 ☐103 ☒Others  
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: \_\_\_\_\_.

Identification of prior art discussed: \_\_\_\_\_.

**Substance of Interview**  
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

During the interview, Attorney indicated that the "37922", cite No. 1 in Sheet 1 of the IDS submitted on 01/19/2015 was not filed correctly and the reference should be strike-out.

**Applicant recordation instructions:** It is not necessary for applicant to provide a separate record of the substance of interview.

**Examiner recordation instructions:** Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/CHU CHUAN (JJ) LIU/ Examiner, Art Unit 3777	
---	--

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/829,352
	Filing Date	July 1, 2010
	First Named Inventor	Jeroen Poeze et al.
	Art Unit	3777
	Examiner	Chu Chuan Liu
SHEET 1 OF 2	Attorney Docket No.	CERCA.002C1

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	<del>1</del>	<del>37,922</del>	<del>03/17/1983</del>	<del>Shim</del>	
	2	4,684,245	08/04/1987	Goldring	
	3	5,122,925	06/16/1992	Inpyn	
	4	5,222,495	06/29/1993	Clarke et al.	
	5	5,625,458	04/29/1997	Alfano et al.	
	6	5,903,357	05/11/1999	Colak	
	7	6,325,761	12/04/2001	Jay	
	8	6,522,521	02/18/2003	Abdul-Hafiz et al.	
	9	6,639,867	10/28/2003	Shim	
	10	6,668,185	12/23/2003	Toida	
	11	6,681,133	01/20/2004	Chaiken et al.	
	12	6,816,010	11/09/2004	Seetharaman et al.	
	13	6,912,413	06/28/2005	Rantala et al.	
	14	7,047,054	05/16/2006	Benni	
	15	7,092,757	08/15/2006	Larson et al.	
	16	7,230,227	06/12/2007	Wilcken et al.	
	17	7,365,923	04/29/2008	Hargis et al.	
	18	7,395,189	07/01/2008	Qing et al.	
	19	7,809,418	10/05/2010	Xu	
	20	7,899,506	03/01/2011	Xu et al.	
	21	8,044,998	10/25/2011	Heenan	
	22	8,126,531	02/28/2012	Crowley	
	23	8,219,170	07/10/2012	Hausmann et al.	
	24	8,332,006	12/11/2012	Naganuma et al.	
	25	8,380,272	02/19/2013	Barrett et al.	
	26	8,421,022	04/16/2013	Rozenfeld	
	27	8,428,674	04/23/2013	Duffy et al.	
	28	8,602,971	12/10/2013	Farr	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English Language Translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

**Appx58304**

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/829,352
	Filing Date	July 1, 2010
	First Named Inventor	Jeroen Poeze et al.
	Art Unit	3777
	Examiner	Chu Chuan Liu
SHEET 2 OF 2	Attorney Docket No.	CERCA.002C1

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	29	8,688,183 (CERCA.008A)	04/01/2014	Bruinsma et al.	
	30	8,909,310 (CERCA.003D1)	12/09/2014	Lamego et al.	
	31	2010/0030040	02/04/2010	Poeze et al.	
	32	2013/0317370 (CERCA.007C1)	11/28/2013	Dalvi et al.	
	33	2014/0066783 (CERCA.006C1)	03/06/2014	Kiani et al.	
	34	2014/0296664 (CERCA.008C1)	03/27/2014	Bruinsma et al.	
	35	2014/0155712 (CERCA.003D1)	06/05/2014	Lamego et al.	
	36	D692,145	10/22/2013	Al-Ali et al.	

FOREIGN PATENT DOCUMENTS						
Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>
	37	WO 2014/149781 (CERCA.082WO)	09/25/2014	Cercacor Laboratories, Inc.		
	38	WO 2014/158820 (CERCA.067WO)	10/02/2014	Cercacor Laboratories, Inc.		

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	39	Japanese Office Action, re JP Application No. 2011-516895, mailed September 2, 2014, with translation. (CERCA.007JP).	√
	40	European Office Action issued in application no. 10763901.5 on 08/27/2014. (CERCA.008EP).	
	41	KANUKURTHY et al., "Data Acquisition Unit for an Implantable Multi-Channel Optical Glucose Sensor", Electro/Information Technology Conference, Chicago, IL, USA, May 17-20, 2007, pp. 1-6	
	42	SMITH, "The Pursuit of Noninvasive Glucose: 'Hunting the Deceitful Turkey'", 2006	
	43	SMALL et al., "Data Handling Issues for Near-Infrared Glucose Measurements", <a href="http://www.ieee.org/organizations/pubs/newsletters/leos/apr98/datahandling.htm">http://www.ieee.org/organizations/pubs/newsletters/leos/apr98/datahandling.htm</a> , accessed 11/27/2007	

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Examiner Signature	/Chu Chuan Liu/	Date Considered	02/08/2016
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

T<sup>1</sup> - Place a check mark in this area when an English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/

Appx58305

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/829,352
	Filing Date	July 1, 2010
	First Named Inventor	Jeroen Poeze et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Chu Chuan Liu
SHEET 2 OF 2	Attorney Docket No.	CERCA.002C1

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Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	29	8,688,183 (CERCA.008A)	04/01/2014	Bruinsma et al.	
	30	8,909,310 (CERCA.003D1)	12/09/2014	Lamego et al.	
	31	2010/0030040	02/04/2010	Poeze et al.	
	32	2013/0317370 (CERCA.007C1)	11/28/2013	Dalvi et al.	
	33	2014/0066783 (CERCA.006C1)	03/06/2014	Kiani et al.	
	34	2014/0296664 (CERCA.008C1)	<del>03/27/2014</del>	Bruinsma et al.	October 2, 2014
	35	2014/0155712 (CERCA.003D1)	06/05/2014	Lamego et al.	
	36	D692,145	10/22/2013	Al-Ali et al.	

Change(s) applied  
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10/13/2015

## FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>
	37	WO 2014/149781 (CERCA.082WO)	09/25/2014	Cercacor Laboratories, Inc.		
	38	WO 2014/158820 (CERCA.067WO)	10/02/2014	Cercacor Laboratories, Inc.		

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	39	Japanese Office Action, re JP Application No. 2011-516895, mailed September 2, 2014, with translation. (CERCA.007JP).	√
	40	European Office Action issued in application no. 10763901.5 on 08/27/2014. (CERCA.008EP).	
	41	KANUKURTHY et al., "Data Acquisition Unit for an Implantable Multi-Channel Optical Glucose Sensor", Electro/Information Technology Conference, Chicago, IL, USA, May 17-20, 2007, pp. 1-6	
	42	SMITH, "The Pursuit of Noninvasive Glucose: 'Hunting the Deceitful Turkey'", 2006	
	43	SMALL et al., "Data Handling Issues for Near-Infrared Glucose Measurements", <a href="http://www.ieee.org/organizations/pubs/newsletters/leos/apr98/datahandling.htm">http://www.ieee.org/organizations/pubs/newsletters/leos/apr98/datahandling.htm</a> , accessed 11/27/2007	

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01192015

Examiner Signature	/Chu Chuan Liu/	Date Considered	03/24/2015
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.			

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PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/829352
	Filing Date	July 1, 2010
	First Named Inventor	Jeroen Poeze
	Art Unit	3777
SHEET 1 OF 2		Examiner Liu,Chu Chuan
		Attorney Docket No. CERCA.002C1

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	5,441,054	08-1995	Tsuchiya	
	2	5,452,717	09-1995	Branigan et al.	
	3	6,636,759	10-2003	Robinson	
	4	2004/0039272	02-2004	Abdul-Hafiz et al.	
	5	2005/0162761	07-2005	Hargis et al.	
	6	2006/0167347	07-2006	Xu et al.	
	7	2006/0189859	08-2006	Kiani et al.	
	8	D551,350	09-2007	Lorimer et al.	
	9	D553,248	10-2007	Nguyen	
	10	D562,985	02-2008	Brefka et al.	
	11	D567,125	04-2008	Okabe et al.	
	12	D569,001	05-2008	Omaki	
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	14	2009/0105565	04-2009	Xu	
	15	7,606,606	10-2009	Laakkonen	
	16	2010/0049018	02-2010	Duffy et al.	
	17	6,278,889	<del>08-2013</del>	Robinson	August 21, 2001

Change(s) applied

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## NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	18	PCT International Search Report, App. No. PCT/US2010/047899, Date of Actual Completion of Search: 01/26/2011, 4 pages.	

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	12/829,352
	Filing Date	July 1, 2010
	First Named Inventor	Jeroen Poeze et al.
	Art Unit	3777
	Examiner	Chu Chuan Liu
SHEET 1 OF 2	Attorney Docket No.	CERCA.002C1

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	37,922	03/17/1983	Shim	
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	4	5,222,495	06/29/1993	Clarke et al.	
	5	5,625,458	04/29/1997	Alfano et al.	
	6	5,903,357	05/11/1999	Colak	
	7	6,325,761	12/04/2001	Jay	
	8	6,522,521	02/18/2003	<del>Abdul Hafiz et al.</del>	Mizuno, et al.
	9	6,639,867	10/28/2003	Shim	
	10	6,668,185	12/23/2003	Toida	
	11	6,681,133	01/20/2004	Chaiken et al.	
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	14	7,047,054	05/16/2006	Benni	
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	16	7,230,227	06/12/2007	Wilcken et al.	
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Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English language translation is attached.

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>  SHEET 2 OF 7	Application No.	12/829352
	Filing Date	July 1, 2010
	First Named Inventor	Jeroen Poeze
	Art Unit	3777
	Examiner	Liu, Chu Chuan
	Attorney Docket No.	CERCA.002C1

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	29	4,755,676	07-1988	Gaalema et al.	
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	31	5,035,243	07-1991	Muz, Edwin	
	32	5,069,214	12-1991	Samaras et al.	
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10/13/2015

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when Can. English or French translation is attached. **ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /CCL/**

CX-1622

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/829352
	Filing Date	July 1, 2010
	First Named Inventor	Jeroen Poeze
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 1 OF 7	Attorney Docket No.	CERCA.002C1

## U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	1	2002/0016536	02-2002	Benni, Paul	
	2	2002/0039272	04-2002	<del>Abdul Hafiz et al.</del>	Mizuno, Shinobu ; et al.
	3	2002/0052547	05-2002	Toida, Masahiro	
	4	2002/0091322	07-2002	Chaiken et al.	
	5	2002/0115918	08-2002	Crowley, Robert J.	
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	7	2006/0167347	07-2006	Xu et al.	
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	19	2008/0139908	06-2008	Kurth, charles dean	
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	21	2009/0043180	02-2009	Tschautscher et al.	
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	24	2010/0049018	02-2010	Duffy et al.	
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Change(s) applied  
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/R.F./  
10/13/2015

Examiner Signature	Date Considered
<p><b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>	

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PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	Unknown
	Filing Date	Herewith
	First Named Inventor	Massi Joe E. Kiani et al.
	Art Unit	Unknown
(Multiple sheets used when necessary)	Examiner	Unknown
SHEET 5 OF 9	Attorney Docket No.	MLHUM.002C1

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	117	6,735,459	05/2004	Parker	
	118	6,728,560	04/2004	Kollias, et al.	
	119	6,725,075	04/2004	Al-Ali	
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	130	6,684,091	01/2004	Parker	
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	132	6,678,543	01/2004	Diab et al.	
	133	6,671,531	12/2003	Al-Ali et al.	
	134	6,661,161	12/2003	Lanzo et al.	
	135	6,658,276	12/2003	<del>Diab et al.</del>	Kiani, et al.
	136	6,654,624	11/2003	Diab et al.	
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	138	6,643,530	11/2003	Diab et al.	
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	141	6,632,181	10/2003	Flaherty et al.	
	142	6,606,511	08/2003	Ali et al.	
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	144	6,597,932	07/2003	Tian et al.	
	145	6,595,316	07/2003	Cybulski et al.	

Change(s) applied  
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/R.F./

10/13/2015

Examiner Signature	Date Considered
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**Appx58311**

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Multiple sheets used when necessary)</i>	Application No.	Unknown
	Filing Date	Herewith
	First Named Inventor	Massi Joe E. Kiani et al.
	Art Unit	Unknown
	Examiner	Unknown
SHEET 8 OF 9	Attorney Docket No.	MLHUM.002C1

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	204	5,860,919	01/1999	Kiani-Azarbayjany et al.	
	205	5,833,618	11/1998	Caro et al.	
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	208	5,810,734	09/1998	Caro et al.	
	209	5,791,347	08/1998	Flaherty et al.	
	210	5,785,659	07/1998	Caro et al.	
	211	5,782,757	07/1998	Diab et al.	
	212	5,769,785	06/1998	Diab et al.	
	213	5,760,910	06/1998	Lepper, Jr. et al.	
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	219	5,638,818	06/1997	Diab et al.	
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	221	5,632,272	05/1997	Diab et al.	
	222	5,602,924	02/1997	Durand et al.	
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	224	5,562,002	10/1996	Lalin	October 8, 1996
	225	5,561,275	10/1996	Savage, et al.	
	226	5,533,511	07/1996	Kaspari et al.	
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	228	5,490,505	02/1996	Diab et al.	
	229	5,482,036	01/1996	Diab et al.	
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	231	5,456,252	10/1995	Vari, et al.	
	232	5,452,717	09/1995	Branigan et al.	

Change(s) applied  
to document,  
/R.F./  
10/27/2015

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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Page 34 of 1082

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**Appx58312**



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/829,352	07/01/2010	Jeroen Poeze	MASCER.002C1	8366
7590 01/04/2016 KNOBBE MARTENS OLSON & BEAR LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614			EXAMINER LIU, CHU CHUAN	
			ART UNIT	PAPER NUMBER
			3777	
			NOTIFICATION DATE	DELIVERY MODE
			01/04/2016	ELECTRONIC

## NOTICE OF NON-COMPLIANT INFORMATION DISCLOSURE STATEMENT

An Information Disclosure Statement (IDS) filed 12-28-15 in the above-identified application fails to meet the requirements of 37 CFR 1.97(d) for the reason(s) specified below. Accordingly, the IDS will be placed in the file, but the information referred to therein has not been considered.

The IDS is not compliant with 37 CFR 1.97(d) because:

- ☒ The IDS lacks a statement as specified in 37 CFR 1.97(e).
- ☐ The IDS lacks the fee set forth in 37 CFR 1.17(p).
- ☐ The IDS was filed after the issue fee was paid. Applicant may wish to consider filing a petition to withdraw the application from issue under 37 CFR 1.313(c) to have the IDS considered. See MPEP 1308.

*NHB*  
571-272-4200 or 1-888-786-0101  
Application Assistance Unit  
Office of Data Management

*FOR*

PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/829352
	Filing Date	July 1, 2010
	First Named Inventor	Jeroen Poeze et al.
	Art Unit	3777
(Multiple sheets used when necessary)	Examiner	Liu, Chu Chuan
SHEET 1 OF 2	Attorney Docket No.	MASCER.002C1

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
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	9	JP 5756752 (MASCER.007JP)	06/05/2015	MASIMO LABORATORIES, INC.		
	10	JP 2002-500908 A	01/15/2002	Lightouch Medical Inc.		Abs
	11	JP 2007-389463 A	11/08/2007	Konica Minolta Sensing Inc.		Abs
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	23	WO 1999/001704	01/14/1999	General Electric Company		

Examiner Signature	Date Considered
<b>*Examiner:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

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PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>	Application No.	12/829352
	Filing Date	July 1, 2010
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SHEET 2 OF 2	Attorney Docket No.	MASCER.002C1

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
	24	Japanese Notice of Allowance, re JP Application No. 2011-516895, issued on May 12, 2015, no translation. (CERCA/MASCER.007JP).	
	25	European Office Action issued in application no. 10763901.5 on August 6, 0015. (CERCA.008EP).	

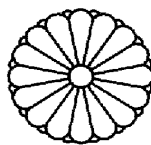
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Examiner Signature	Date Considered
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T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.



CX-1622



# 特 許 証

(CERTIFICATE OF PATENT)

特許第5756752号  
(PATENT NUMBER)

発明の名称  
(TITLE OF THE INVENTION)

センサ

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登録日  
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その他別紙記載

この発明は、特許するものと確定し、特許原簿に登録されたことを証する。  
(THIS IS TO CERTIFY THAT THE PATENT IS REGISTERED ON THE REGISTER OF THE JAPAN PATENT OFFICE.)

平成27年 6月 5日(June 5, 2015)

特許庁長官  
(COMMISSIONER, JAPAN PATENT OFFICE)

伊藤



CX-1622

# 特 許 証

(CERTIFICATE OF PATENT)

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特許第5756752号 (PATENT NUMBER)

特願2011-516895 (APPLICATION NUMBER)

発明者  
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## 特許権設定登録通知書

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請求項の数 9

納付年分 第 3年分まで

受領金額 12,300円

受領日 平成27年 6月 1日

## 重要 特許料の納付について

・特許権を維持するには、存続期間の満了（特許出願の日から20年）までの各年について所定の特許料の納付が必要です。

なお、**第4年分以降の納付に関しては、特許庁から納付についての通知は送付いたしませんので、納付期限の管理はご自身でお願いいたします。**

この通知を保管し、右側の特許料納付期限日の表で納付期限を確認していただきます。（**自動納付制度**もありますので、特許庁ホームページを参照してください。）

・第4年以降の各年分の特許料は、登録日の翌日を起算日として、納付済年分の満了日（以下「納付期限日」という）までに、次の年分の納付が必要です。

・納付期限日までに納付できなかつたときは、その期間の経過後6ヶ月以内であれば特許料を追納することができま

・追納する場合は、納付すべき特許料のほか、その特許料と同額の割増特許料が必要

です。

・追納できる期間内に納付しないときは、その特許権は、納付期限日にさかのぼって消滅したものとみなされます。

・特許料納付書の様式及び特許料の額については、以下を参照してください。

特許庁ホームページ

<http://www.jpo.go.jp/index.j.htm>

## 特許料納付期限日

納付年分	納付期限日
第 4 年分	平成30年 6月 5日
第 5 年分	平成31年 6月 5日
第 6 年分	平成32年 6月 5日
第 7 年分	平成33年 6月 5日
第 8 年分	平成34年 6月 5日
第 9 年分	平成35年 6月 5日
第10年分	平成36年 6月 5日
第11年分	平成37年 6月 5日
第12年分	平成38年 6月 5日
第13年分	平成39年 6月 5日
第14年分	平成40年 6月 5日
第15年分	平成41年 6月 5日

(注) 納付期限日が行政機関の休日にあたるときは、その日の翌日間の末日となります。

問い合わせ先 審査業務課登録室  
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Espacenet

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## METHOD AND DEVICE FOR TISSUE MODULATION

**Inventor(s):**

**Applicant(s):**

**Classification:** - international: A61B10/00; A61B5/00; A61B5/024; A61B5/145; A61B5/1455; G01N21/17; G01N21/65; (IPC1-7): A61B10/00; A61B5/145; G01N21/17; G01N21/65  
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**Application number:** JP20000528203 19990127

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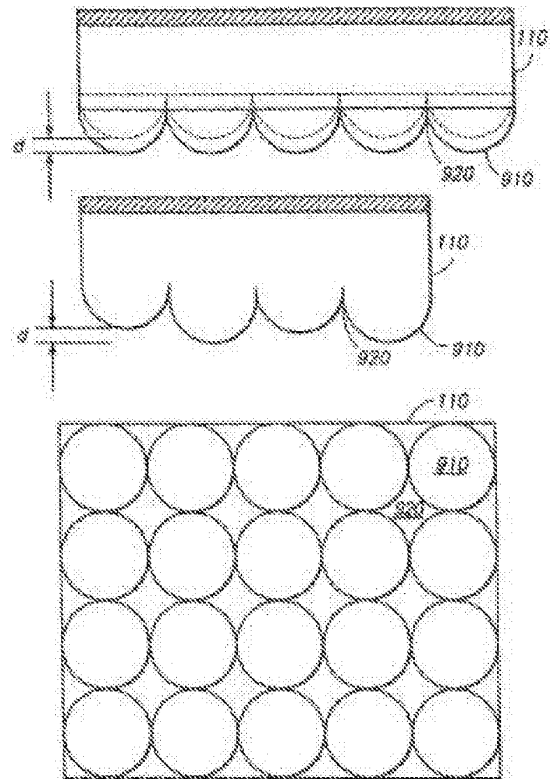
**Also published as:** WO9937205 (A1) WO9937205 (A8) CA2315192 (A1) CA2315192 (C) US6223063 (B1) more

Abstract not available for JP2002500908 (A)

Abstract of corresponding document: WO9937205 (A1)

A tissue modulation device comprises an upper surface and a lower surface, the upper surface comprises a recessed region (920) adjacent to a raised region (910), wherein application of a first portion of a tissue relative to a second portion of the tissue that is in apposition to the recessed region (920). An optically transparent region of the device is curved at the lower surface to substantially reduce backscattered light in a light path traveling through the optically transparent region to a light collection system. A method of noninvasive spectroscopic measurement of an analyte in a subject comprises applying tissue of the subject to the tissue modulation device so that the raised region depresses a first portion of tissue relative to a second portion of tissue in apposition to the recessed region; irradiating the tissue in a blood-replete and a blood-depleted state with electromagnetic radiation; and analyzing the collected spectra to determine a concentration of analyte present in the tissue, by determining the difference between the spectra of the blood-replete and blood-depleted states.

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 (33) 優先権主張国 米国 (US)  
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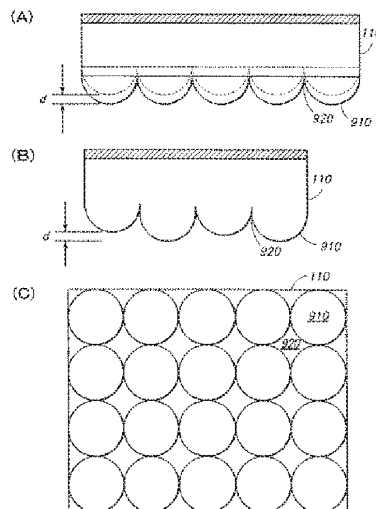
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(54) 【発明の名称】 組織変調装置およびその方法

(57) 【要約】

【課題】 周囲組織と対比して血液に帰する信号を分離するための非侵襲的な血液分析方法を提供すること。

【課題手段】 組織変調装置は高位表面と低位表面とを含み、高位表面は高所領域910と隣接の凹所領域920とを含む。組織の第1の部分の高所領域への適用は、凹所領域920と同様の組織の第2の部分に対して相対的に組織の第1の部分を押圧する。装置の光学的に透明な領域は、光学的に透明である領域を通して光収集系に進む光路において後方散乱光を実質的に減少させるために低位表面で曲げられる。方法は、生体の組織を高所領域と隣接の凹所領域を含む組織変調装置に適用すること、血液充満および枯渇状態の組織に励起波長を有する電磁放射線を照射し放出されたスペクトルを収集すること、検体濃度決定のために血液充満および枯渇状態とで収集されたスペクトル間の相違を決定することを含む。



(2) 002-500908 (P2002-500908A)

## 【特許請求の範囲】

【請求項 1】 高位表面と低位表面とを含む組織変調装置であって、  
前記高位表面は高所領域と隣接の凹所領域を含み、  
前記装置は前記凹所領域または前記高所領域の少なくとも一方が光学的に透明であり、

組織の第 1 の部分の前記高所領域への適用は、前記凹所領域と同格である前記組織の第 2 の部分に対して相対的に前記組織の第 1 の部分を押圧することであり、

前記装置の光学的に透明である領域は、前記光学的に透明である領域を通して光収集系に進む光路において後方散乱光を実質的に減少させるために低位表面で曲げられる、組織変調装置。

【請求項 2】 前記高所領域は不透明である、請求項 1 に記載の装置。

【請求項 3】 前記高所領域は光学的に透明である、請求項 1 に記載の装置。

【請求項 4】 前記凹所領域は光学的に透明である、請求項 1 に記載の装置。

【請求項 5】 前記凹所領域は前記装置の前記高位表面の隣接部分に対して相対的に凹状に形成される、請求項 1 に記載の装置。

【請求項 6】 前記光学的に透明な領域はさらに光学フィルタを含む、請求項 1 に記載の装置。

【請求項 7】 前記光学的に透明な領域は光収集系を含む、請求項 1 に記載の装置。

【請求項 8】 前記光収集系はレンズを含む、請求項 7 に記載の装置。

【請求項 9】 前記レンズはレーザによって放出された光を前記組織に合焦させることができる、請求項 8 に記載の装置。

【請求項 10】 前記レンズは前記組織によって放出された光を検出器に合焦させることができる、請求項 8 に記載の装置。

【請求項 11】 前記光収集系は光ファイバ収集器を含む、請求項 7 に記載の装置。

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【請求項 12】 前記光収集系は複数のレンズを含む、請求項 7 に記載の装置。

【請求項 13】 前記レンズは屈折率を異なって形成される、請求項 12 に記載の装置。

【請求項 14】 実質的に曲げられた表面は凸状である、請求項 1 に記載の装置。

【請求項 15】 実質的に曲げられた表面は凹状である、請求項 1 に記載の装置。

【請求項 16】 実質的に曲げられた表面は約 2 cm 未満の曲率半径を有する、請求項 1 に記載の装置。

【請求項 17】 実質的に曲げられた表面は約 7 mm の曲率半径を有する、請求項 1 に記載の装置。

【請求項 18】 複数の高所領域を含む、請求項 1 に記載の装置。

【請求項 19】 前記高所領域は高さを異なって形成される、請求項 18 に記載の装置。

【請求項 20】 生体の外部組織の前記装置への適用において、少なくとも第 1 の高所領域は血液を含む前記組織の部分に光を合焦させ、少なくとも第 2 の高所領域は皮膚を含む前記組織の部分に光を合焦させる、請求項 18 に記載の装置。

【請求項 21】 前記高所領域の端部は約 20  $\mu$ m から約 200  $\mu$ m 離隔する、請求項 18 に記載の装置。

【請求項 22】 前記高所領域は約 50  $\mu$ m から約 2 mm の高さである、請求項 1 に記載の装置。

【請求項 23】 さらに複数の凹所領域を含む、請求項 18 に記載の装置。

【請求項 24】 約 8 mm 未満の直径を有する、請求項 1 に記載の装置。

【請求項 25】 前記直径は約 4 mm から約 5 mm である、請求項 24 に記載の装置。

【請求項 26】 前記高位表面と前記低位表面との間の厚さが約 3 mm 未満である部分を少なくとも有する、請求項 1 に記載の装置。



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【請求項 27】 電磁放射線源と光検出器とに光学的に結合される、請求項 1 に記載の装置。

【請求項 28】 連続した輪を形成するように連結された一続きの交互配置の凹所領域および高所領域と、少なくとも 1 つの回動可能なスプロケットであって前記スプロケットの回動が前記輪の回動をもたらすように前記輪と関係するスプロケットとを含む、請求項 1 に記載の装置。

【請求項 29】 前記高所領域は実質的に円筒状または円柱状のローラを含む、請求項 28 に記載の装置。

【請求項 30】 前記凹所領域は第 1 の端部と第 2 の端部とを有する長さを含み、さらに、前記凹所領域は実質的に長方形の断面を有し、実質的に円形の断面を有する部分と端部で隣接する、請求項 28 に記載の装置。

【請求項 31】 生体中の検体の非侵襲的な分光測定のための組織変調方法であって、

(a) 生体の組織を、高所領域は凹所領域と同格の前記組織の第 2 の部分に対して相対的に前記組織の第 1 の部分を押圧するように、前記高所領域と隣接の前記凹所領域を含む組織変調装置に適用すること、

(b) 血液充满状態の組織に励起波長を有する電磁放射線を照射すること、

(c) 前記血液充满状態の組織によって放出されたスペクトルを収集すること、

(d) 血液枯渇状態の組織に励起波長を有する電磁放射線を照射すること、

(e) 前記血液枯渇状態の組織によって放出されたスペクトルを収集すること、

(f) 前記組織中に存在する検体の濃度を決定するために前記収集されたスペクトルを分析することであって前記血液充满状態と前記血液枯渇状態とで収集されたスペクトル間の相違を決定することを含んで分析することを含む、組織変調方法。

【請求項 32】 前記スペクトルはラマン・スペクトルである、請求項 31 に記載の方法。

【請求項 33】 前記組織の第 1 の部分において前記血液枯渇状態を達成す

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るために十分な圧力で前記組織は前記装置に適用される、請求項 31 に記載の方法。

【請求項 34】 前記組織の第 2 の部分において前記血液充滿状態を達成するために十分な圧力で前記組織は前記装置に適用される、請求項 31 に記載の方法。

【請求項 35】 前記血液充滿状態および前記血液枯渇状態は、前記組織が前記装置に適用される圧力量を変化させることによって前記組織の第 1 の部分において達成される、請求項 31 に記載の方法。

【請求項 36】 前記血液充滿状態および前記血液枯渇状態は、前記高所領域および前記凹所領域を前記組織の第 1 の部分に交互に適用することによって前記組織の第 1 の部分において達成される、請求項 31 に記載の方法。

【請求項 37】 前記凹所領域は前記装置の隣接表面に対して相対的に凹状に形成される、請求項 31 に記載の方法。

【請求項 38】 前記凹所領域は前記装置を通る経路を含み、該経路を通じて前記組織は照射される、請求項 31 に記載の方法。

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## 【発明の詳細な説明】

## 【0001】

## 【発明の属する技術分野】

本発明は、組織中の血液の流れを変調 (modulating) するための方法および装置に関する。関係する毛細血管床中の血液の流れおよび存在に作用するために機械的圧力が組織領域に適用される。この方法は血液検体の非侵襲的測定を容易にする。

## 【0002】

種々の刊行物は本出願の至る所に引用されている。これによって、これらの公表物全体の開示は、本発明が属する技術の態様をより十分に記載するために本出願へ引用されることによって本出願に組み込まれる。

## 【0003】

## 【従来の技術】

長い間、生体化学作用の非侵襲的な計測管理にかなりの関心がもたれてきた。米国には1600万人の糖尿病患者がおり、血糖値 (血中グルコース濃度) の非侵襲的な測定方法が実現すれば、患者全員が恩恵を被ることになる。現在広く採用されている血糖値の測定方法を用いた場合は、多くの糖尿病患者は、該患者のインシュリン要求条件を適切に計測管理するために、日に5回から7回の血液採取をしなければならない。血中グルコースの非侵襲的な測定により、さらに精密な制御を課すことができ、糖尿病がもたらす継続的な損傷、障害および費用は最小限になる。

## 【0004】

血液酸素測定法は、含酸素血液と脱酸素血液との間の均衡を非侵襲的に計測管理する電子吸収分光法の応用例である (1997年4月1日付け発行の米国特許第5,615,673号)。同様に、振動分光法は、複雑な混合物を定量的および定性的に半ピボ分析する信頼のおける方法であり、代謝作用として関係する重要な検体に対して、この方法を試験管内で応用した報告がある (エス・ワイ・ワン (S. Y. Wang) 他、1993年、レーザ・ラマン分光法による水様液の代謝産物の分析、応用光学32(6):925-929; エー・ジェー・バーガー (A.

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J. Berger) 他、1996、近赤外ラマン分光法による水様性生物学的検体の迅速な非観血的濃度測定、応用光学35(1):209-212)。振動吸収分光法のような赤外線測定は人の皮膚組織に應用されている。しかし、赤外線測定は、その波長域で適した光源や検知器の入手が不可能であり、また、入射放射線の吸収に基づく組織の加熱作用のため、測定の成功率が制限されるものであった(米国特許第5,551,422号、また、アール・アール・アンダーソン(R. R. Anderson)およびジェー・エー・パリッシュ(J. A. Parrish)、1981年、人の皮膚光学(The Optics of Human Skin)、ジェー・調査皮膚病学(J. Investigative Dermatology)77(1):13-19)。血中グルコースの非侵襲的な計測管理方法を提供する従来の試みは、1996年9月10日付け発行の米国特許第5,553,616号に要約されている。

## 【0005】

血液分析に対して非侵襲的な技術を最適に適用するには、周囲の組織と対比して血液に帰する信号を分離するための改善された方法が要求される。

## 【0006】

## 【課題を解決するための手段】

本発明は、血液検体に関する信号を取得するためのこの要求を満たす装置および方法を提供する。本発明は、高位表面と低位表面とを含む組織変調装置であって、高位表面は高所領域と隣接の凹所領域を含み、装置は凹所領域または高所領域の少なくとも一方が光学的に透明であり、組織の第1の部分の高所領域への適用は、凹所領域と同格である組織の第2の部分に対して相対的に組織の第1の部分を押圧することであり、装置の光学的に透明である領域は、光学的に透明である領域を通して光収集系に進む光路において後方散乱光を実質的に減少させるために低位表面で曲げられる、組織変調装置を提供する。一実施例において、高所領域は不透明である。他の実施例において、高所領域は光学的に透明である。一実施例において、凹所領域は光学的に透明である。凹所領域は、装置の高位表面の隣接部分に対して相対的に凹状に形成されることができる。

## 【0007】

一実施例において、装置は、さらに、連続した輪を形成するように連結された

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一続きの交互配置の凹所領域および高所領域と、少なくとも1つの回転可能なスプロケットであってスプロケットの回転が輪の回転をもたらすように輪と関係するスプロケットとを含む。高所領域は実質的に円筒状または円柱状のローラを含むことができる。凹所領域は第1の端部と第2の端部とを有する長さを含むことができ、さらに、凹所領域は、実質的に円形の断面を有する部分と一端部で隣接して、実質的に長方形の断面を有することができる。

## 【0008】

本発明はさらに生体中の検体の非侵襲的な分光計測の方法を提供する。本方法は、凹所領域と同格の組織の第2の部分に対して相対的に高所領域は組織の第1の部分を押圧するように、生体の組織を、高所領域と隣接の凹所領域を含む組織変調装置に適用することを含む。さらに本方法は、血液充満状態の組織に励起波長を有する電磁放射線を照射し、血液充満状態の組織によって放出されたスペクトルを収集することを含む。さらに本方法は、血液枯渇状態の組織に励起波長を有する電磁放射線を照射し、血液枯渇状態の組織によって放出されたスペクトルを収集することを含む。収集されたスペクトルは、組織中に存在する検体の濃度を決定するために分析される。分析は、血液充満状態と血液枯渇状態とで収集されたスペクトル間の相違を決定することを含む。このスペクトルは好ましくはラマン・スペクトルである。他のスペクトルの例として、NMR、ESR、UV可視吸収、IR吸収、蛍光、燐光スペクトルが含まれが、これらに限定されるものではない。

## 【0009】

## 【発明の実施の形態】

組織変調装置は、分光計測のような測定が血液充満と血液枯渇の両状態において行われ得るように、本方法が適用される組織を処理することに関係する。組織変調のための一方法は、指先のような組織の領域に圧力を適用することである。圧力が適用されると組織の領域は血液枯渇の状態にされる。圧力が解放または低減されると、血液は、いま影響を受けた組織に戻る。仮骨、排泄物、せっけん残余、および周囲の組織に関係するその他の出現物による外部スペクトル信号の影響を最小限にする場合において、血液充満状態と血液枯渇状態とで行われる測定

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間の相違は、血液中の元素を示す測定を提供する。組織変調が非侵襲的な分光法において行われるとき、例えば、分析は、血液充満と血液枯渇との状態において収集されたスペクトル間の相違を決定することを含むことができる。

【 0 0 1 0 】

定義

【 0 0 1 1 】

本出願において用いる科学のおよび技術的用語は、他に規定されない限り、本発明の属する技術の分野において一般に用いられる意味を有する。本願で用いられる場合、以下の語や句は特定の意味を有する。

【 0 0 1 2 】

本願で用いる場合、「組織」は、生体の臓器や系統のどの部分でもよく、皮膚、毛細血管床、血液、筋肉、胸部、脳を含むが、これらに限定されない。

【 0 0 1 3 】

本願で用いる場合、「所定の成分に関係するラマン・スペクトル」は、その成分が放出するラマン・スペクトルを指し、ラマン・スペクトルは、本発明の属する技術の分野における通常の知識を有する者が、ラマン・スペクトルの発生原因をその成分に帰することができるものである。相対的に純粋な形で前記成分に放射線を照射し、他の成分が相対的に存在しない場合の前記成分によって放出されるラマン・スペクトルを収集且つ分析することによって、ラマン・スペクトルは所定の成分に帰することを決定できる。

【 0 0 1 4 】

本願で用いる場合、「血液充満」は、血液が組織を流れて流れる状態が遮断されないことを指し、例えば、冷却または圧力作用により誘発される血管狭窄がないことを指す。血液充満の状態は加熱のように血管拡張を増進させる条件によって増強され得る。

【 0 0 1 5 】

本願で用いる場合、「血液枯渇」は、血液が組織を流れて流れる状態が実質的に制限され血液量が最小化することを指す。血液枯渇の状態は、例えば、組織に対して冷却および／または圧力作用によって達成できる。

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## 【0016】

本願で用いる場合、「不透明」は、光が物体を通過することを実質的に妨げるようなその物体の光学的特性を指す。組織変調装置の好適な実施例においては、いかなる光も不透明領域を通過しない。

## 【0017】

本願で用いる場合、「光学的に透明」は、光が物体を通過することを許可されるようなその物体の光学的特性を指す。

## 【0018】

本願で用いる場合、「組織の部分」は、光が進む組織領域を指し、この領域から信号が収集される。

## 【0019】

本願で用いる場合、「凹所領域」は、高所領域に対して相対的に凹状に形成された領域を指し、すぐ近くの周囲表面に対して相対的に凹状に形成されてもされなくてもよい。

## 【0020】

発明の方法

## 【0021】

本発明は、1以上の血液検体が示す1以上の信号の測定と同時に血液量の測定の方法を提供する。血液量の測定は、濃度値の計算を可能にするために血液検体測定の標準化を可能にする。温度と圧力とは、毛細血管の内容物に作用させるために用いることができ、温度と圧力は大部分は制御することができるが、組織変調装置を標準化の目的で用いることは好ましい。本発明は、個々の分析と血液の流れの型との間の相違による誤差に影響されない標準化のための方法を提供する。

## 【0022】

本発明は、生体中の検体の非侵襲的な分光測定の方法を提供する。一実施例において、本方法は、凹所領域と同格の組織の第2の部分に対して相対的に高所領域は組織の第1の部分を押圧するように、生体の組織を、高所領域と隣接の凹所領域を含む組織変調装置に適用することを含む。さらに本方法は、血液充满状態

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の組織に励起波長を有する電磁放射線を照射し、血液充満状態の組織によって放出されたスペクトルを収集することを含む。さらに本方法は、血液枯渇状態の組織に励起波長を有する電磁放射線を照射し、血液枯渇状態の組織によって放出されたスペクトルを収集することを含む。さらに本方法は、組織中に存在する検体の濃度を決定するために収集されたスペクトルを分析することであって血液充満状態と血液枯渇状態とで収集されたスペクトル間の相違を決定することを含んで分析することを含む。収集されうるスペクトルの例として、ラマン、核磁気共鳴（NMR）、電子スピン共鳴（ESR）、UV可視吸収、赤外吸収、蛍光、燐光スペクトルが含まれるが、これらに限定されるものではない。

## 【0023】

一実施例において、高所領域と接触する組織の第1の部分の血液枯渇状態を達成するために、組織は十分な圧力で装置に適用される。組織が適用される圧力は、装置の凹所領域と接触する組織の第2の部分において血液充満状態が同時に達成されるような圧力である。他の実施例において、血液充満状態と血液枯渇状態とは、組織が装置の高所領域に適用される圧力量を変化させることによって、組織の第1の部分において異なる時点で達成される。他の実施例において、血液充満状態と血液枯渇状態とは、高所領域と凹所領域とを組織の第1の部分に選択的に適用することによって、組織の第1の部分において達成される。

## 【0024】

本方法の異なった実施例に適應させるために、本装置の種々の変更を行うことが可能である。例えば、凹所領域は装置の隣接表面に対して相対的に凹状に形成されることができる。この変更は、凹所領域に適用される組織中の血液充満状態の達成を容易にすることができる。他の実施例において、組織が経路を介して照射され得るように、凹所領域は装置を通過する経路を含む。装置内の経路の供給は、組織と本方法に共同して用いられる光収集および／または検出系との間と同様に、組織を照射するために用いられる光源と照射された組織との間の障害のない光路を可能にする。

## 【0025】

好適な実施例において、組織は指先のような毛細血管床を循環する血液の十分



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な供給を有する。他の組織として、例えば、耳たぶ、筋肉、皮膚、胸部、脳とすることができる。生体は好ましくは哺乳類、鳥類、爬虫類、魚類のような脊椎動物である。哺乳類の例として、人、牛、豚、羊、ネズミ、馬、犬、猫が含まれるが、これらに限定されるものではない。最も好適な実施例においては、生体は人である。

## 【0026】

組織変調装置

## 【0027】

ここに開示された発明は、組織中の血液の流れを変調するために用いることのできる装置を提供する。本装置は、組織中の検体を測定するための方法と組み合わせ用いることに適している。本装置は非侵襲的に用いることができる。本装置は高位表面と低位表面とを含む。高位表面は1以上の高所領域と隣接の1以上の凹所領域を含む。該凹所領域は、装置の高位表面に合流するまたは高位表面に対して相対的に凹状に形成されることができる。組織の一部分を装置の高所領域に適用することは組織の他の隣接部分に対して相対的に前記組織の一部分を押圧することであるように、高所領域は高位表面から突出する。

## 【0028】

一実施例において、高所領域は装置の高位表面から約50  $\mu\text{m}$  から約2 mm 突出する。好ましくは、高所領域は高位表面から約100 から約300  $\mu\text{m}$  突出する。本装置は、高さの異なる複数の高所領域を含む単一の高所領域または複数の高所領域を有することができる。さらに、本装置は、該装置の高位表面に対して相対的に凹状に形成される範囲内において選択的に変化させることのできる複数の凹所領域を有することができる。高所領域および凹所領域は、他方にすぐ隣接するまたは間隔をおいて離隔することができる。好ましくは、凹所領域および／または高所領域は約20  $\mu\text{m}$  から約2 mm 離隔する、さらに好ましくは約750  $\mu\text{m}$  離隔する。

## 【0029】

好適な実施例において、本装置は直径が約8 mm 未満である。さらに好ましくは、本装置の直径は約4 mm から約5 mm である。本装置の少なくとも部分の高

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位表面と低位表面との間の厚さは約3 mm未満である。

#### 【0030】

少なくとも1つの凹所領域および／または少なくとも1つの高所領域は光学的に透明である。本装置の光学的に透明な領域は、光学的に透明な領域を通して光収集系に進む光路において後方散乱光を実質的に減少させるために低位表面で曲げられる。本装置は、電磁放射線源および／または光検出器に光学的に結合されることができる。一実施例において、本装置は、1以上のレンズを含むことができる光収集系を含む。好適な実施例において、レンズまたは他の光収集系は、装置の1以上の高所領域に組み合わされる。他の実施例において、本装置は、光源を用いて組織を照射するための手段および／または照射された組織によって放出された光を収集し検出するための手段とを選択的に含む装置または系の部分である。1以上のビームスプリッタ、選択的なレンズ、フィルタおよびコリメータは、組織に入出する光を変更するための光路に案内される。

#### 【0031】

図1に示すように、検出器140は、組織変調装置110に組み合わされて用いることができる。複数の検出器は、単一の組織変調装置とともに用いるために統合されることができる。一実施例において、光を各検出器に個別に映すことができるように、四分円検出器140は単一の小基板に配された4つの感光検出器160を有して用いられる。レーザ130からの光は、光が皮膚のような表面を通る組織100の領域へ指向される。この実施例において、送出光は特有のスペクトル幅と入射光波長以外の波長とを有することができる。この送出光が検出器160に衝突すると、その光によって調達された電力に比例して電流が発生される。

#### 【0032】

四分円検出器140に光学的に整列される4つのオプト・メカニカル要素150の各要素は、選択された量の組織変調に各要素が同時に従属される間、同時に用いられることができる。用いられる組織変調の型は、四分円検出器140の4つの検出器160の各々間で行われる組み合わせを定義することができる。これらの組み合わせは、血液枯渇領域から検出器へ到達する信号量を血液充満領域か

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ら同時に放出する信号量から差し引くように設計される。

#### 【0033】

好ましくは、信号のデジタル化または増幅の前に、信号はアナログ領域にある間において減算される。このことは、信号減算の前に血液枯渇または血液充満の組織領域から放出する信号を増幅およびデジタル化することによって得られる結果と比較して、雑音に対する改善信号と改善ダイナミック・レンジとを与える。デジタル化の前に信号を減算することの利点は、環境変動に関する雑音と供給電力とが各検出器に対して同じであるように、各検出器は同じ基板上にあり、それゆえ同じ供給電力により偏倚されることである。雑音は単純なアナログ減算によって改善される。検出器と増幅／減算回路構成要素とは同じチップ上に組み合わせられるので、これらの異なる検出器によって発生される電流中に存在する多くの雑音が関係づけられるように、増幅部の負荷抵抗のような構成要素を供用するために設計および製造することができる。雑音は直接にフィルタ処理して取り除くことができ、減算前の雑音の増幅が回避される。信号をデジタル化し減算することは、血液充満領域からの信号と血液枯渇領域からの信号との間の相違における雑音の増加に至る。

#### 【0034】

前記の四分円検出器の実施例は、用いる光源の電力出力の変動を表す手段を用いて組織変調の空間的に別個な領域の同時発生を単一要素に統合する。この実施例においては、単一光源は、入射光の同じ変動量を同時に感知する4つの別個の領域を発生することができる。

#### 【0035】

図2は、組織変調器110と光源130とに結合された四分円検出器140を示す図である。この図において、斜線を付した円および付していない円は、光源130から放出される整列した平行光線によって尋問される血液充満および血液枯渇の領域を示す。AおよびDによって示される血液充満領域から放出される信号は、BおよびCによって示される血液枯渇領域からの信号と同様に、検出器140の対応する四分円に映される。四分円検出器140は、以下の過程が生じるように結線される。

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## 【0036】

全四分円検出器出力 = (A + D) - (B + C) = (血液充満領域からの全信号) - (血液枯渇領域からの全信号) = (血液からの信号)。

## 【0037】

光源130からの光は、非反射コートを施された変調器110の後方側へ全反射されるようにビームスプリッタ120に当たる。ビームスプリッタ120は残余の後方反射が分岐されるように形作られる。このことは、ビームスプリッタ120を通り、分光写真機／偏光子／ノッチ・フィルタを通過して四分円検出器140に指向される光源の光量を最小にする。

## 【0038】

変調器の背面を通過する光は、変調器110の前部の形状によって、図2に示される血液の充満および枯渇の領域に合焦される。変調器の前面を通過する光は、相互作用領域（図2の線の交点によって示される）の組織から散乱し、散乱光の一部は、散乱光を変調器110の前面に再入射させる曲線を有する。これらの光線は、再視準され、ビームスプリッタ120へ送り戻される。これらの光線は、ビームスプリッタ120を通過して、分光写真機／偏光子／ノッチ・フィルタを通過して四分円検出器140に進む。

## 【0039】

図2に示す実施例において、平行光線の組は、変化する領域を走査する区域を照明する。血液充満および枯渇領域は、組織変調器110と指先100または測定に用いられる生体の他の部分との間での機械的接触によって作られる。変調器110の形状は、単一の一本石に合併される4つの球レンズが存在するように設計される。血液枯渇領域（BおよびCによって示される）を作る球の中心は、この中心が指先100を用いて接触が行われる点から外へ血液を押圧するために十分に突出する（少なくとも約200ミクロン）ように、変調器110の中心から外方へ移動される。この同じ位置で、他の2つの球（AおよびBによって示される）は、それらの隣接組織から外へ血液を押圧するために十分な接触を行わない。

## 【0040】

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前記に示された接近は、第1の光源からの後方散乱光の排除、組織変調されたスペクトル信号、および雑音を最小にし信号を増大させる自動アナログ信号処理を達成する。

## 【0041】

静的組織変調

## 【0042】

生体組織領域の血液の流れを変調するための方法は、時間に関して変動しない機械的圧力または他の物理的圧力を適用することを含む。本願においては、この方法を静的組織変調として言及する。静的組織変調の間、尋問される領域の血液内容は、測定が行われる間可能な限り一定に保たれる。3つの測定を行うことができる。すなわち、血液量が表示される測定、生体の検体に関連する測定、および生体の組織への光学的結合の質を評価するために非干渉波長で行われる測定である。最初の2つの測定の比率は、3番目の測定を用いて標準化され、検体濃度に比例する。比例関係の一定性は、各使用者に対して個別に決定され得る。

## 【0043】

静的組織変調のために設計された実施例において、光学要素は、組織変調を実現するために用いられる表面に結合される。一実施例において、図4に示すように、レンズは、組織変調装置110の高位表面から突出する高所領域150に統合されている。図4に示す実施例において、単一の平凸レンズが用いられる。異なるレンズは、所望の光学および機械的特性に従って設計に合併される。ここに記載する例は、屈折光学部品に基いている。本発明の属する技術の分野における通常の知識を有する者は、回折光学部品もまた装置に合併され得ることが容易に理解される。

## 【0044】

皮膚と接触する表面に報いて、圧力は組織変調に典型的に適用される。この表面は、有利な屈折特性および／または空間的に符号化された圧力に対応する皮膚の空間的な符号化に表面を用いる方法で選択されることができる。第1の光学的な収集表面としてのこの表面の使用は、最も効率の良い光収集を可能にする。なぜなら、この使用は、露出した組織表面と光収集系の第1の表面との間の距離と

(註7) 102-500908 (P2002-500908A)

同様に光学的表面の数を最小にする。

#### 【0045】

複数の光学的に透明な領域を有する装置は、組織の空間的に個別な領域からの情報を符号化することを可能にする。空間的な符号化は、1つの空間的な位置と他との間の対照によって示される差異を提供することができ、各位置は、圧力（組織変調）の異なった量を受け取り、露出した組織の単位区域当たりの血液量を示す異なった信号を提供する。図1は、光学的表面として第1の表面を用いる系の一例を与える。図3の（A）および（B）は、空間的な符号化感知から有用である数少ない方式を提案する。例えば、四分円検出器は、等しい最小の正方形の格子上に4つの検出器が配置される位置に存在し、格子は組織変調位置として作動する小レンズの配置を模倣する。四分円検出器において固有の検出器雑音の原因となる要因は、位置の空間的な近接によりすべての異なる空間的な位置が等しくなる傾向である。減算測定は、検出器雑音を相殺する検出器を用いることに接近する。

#### 【0046】

図5から図7は、光路を変更するために用いられ得る組織変調装置110の種々の実施例を示す。図5および図6は、偏光ビームスプリッタ120とさらに合焦要素160とに統合されている装置110を示している。これらの変更は、同時映写の使用と波長の組み合わせとに適合されている。図7は、装置110の使用に対して円筒状または円柱状のレンズ710から750の変更がある。加えて、アダマール符号化および精巧な信号処理を達成するために輻が変化する複数の円筒状または円柱状のレンズを統合することができる。共焦点技術の使用は、皮膚表面効果および電磁線放射線の増大を排除する焦点深度と、毛細血管床へおよび毛細血管床から進む光の収集効率とを可能にする。光が通って指向される高所領域の高さを変更することによって、光を合焦させ、1つの高さをを用いる皮膚および第2の高さをを用いる血液から測定を行うことができる。

#### 【0047】

動的組織変調

#### 【0048】

(註 8) 102-500908 (P2002-500908A)

ある実施例において、組織変調装置は、異なる時点で組織の所定の領域から情報が得られるように設計される。本願では、この方法を動的組織変調として言及する。動的組織変調において、所定の応力および／または圧力の量が組織に適用され、その後解放または低減される。尋問された組織の血液の平衡分布が通常循環で復旧する時間において、測定は行われる。濃度測定 of 構成要素、すなわち検体関係の信号および血液量関係の信号は、信号の変化と血液量の変化とを関係づけるための測定を処理することによって得られる。

【 0 0 4 9 】

動的組織変調方法の利点は、血液流とともに変化する信号を、血液流が変化すると一定のままとなる非血液関係信号から区別することによって達成される血液関係信号の増幅である。加えて、一時的または動的変調は、高精度かつ正確な検体測定を相当に改善するために、空間的な符号化と結合される。

【 0 0 5 0 】

本発明は、動的組織変調のための装置を提供する。装置は、組織の領域を血液枯渇にさせる手段と、血液枯渇の原因を解放する手段、および組織領域の血液枯渇の前、間および後の組織の領域の分光的尋問の手段とを含む。ある実施例は、さらに、光学的に透明な板材であって血液を隣接の毛細血管床から移動させるために板材が皮膚表面に対する十分な圧力を作用することのできる位置に配する手段を含む。そのような板材は、空間的に選択される組織変調をもたらすために、高所および凹所領域を含む。

【 0 0 5 1 】

血液枯渇を発生させ、その後解放する方法は、1 以上のスプロケットの回りを移動する連続した一続きの回路または搬送ベルト形状の使用を含む。板材は位置が回転させられ、組織の血液枯渇領域を達成するように指または他の組織は板材に配される。スプロケットを回転させることによって、ベルトはすばやく例えば 0.2 秒またはそれ未満で横に移動させられる。この移動は、以前の血液枯渇領域に血液を流れ戻らせることを可能にする。この過程において、尋問された光は変調された組織に衝突することができ、分光計測を行うことができる。適用された圧力量は、少なくとも約 1 から約 100 g / cm<sup>2</sup>、好ましくは約 1 kg / c

(図9) 102-500908 (P2002-500908A)

m<sup>2</sup>を越えない範囲である。

#### 【0052】

組織変調前、間および後の分光計測を可能にするために、搬送ベルトの隣接板材は、不透明または透明であるように、または構造において間隙を有するように選択されることができる。不透明な板材は、血液枯渇状態に対応して圧力が移動された後すぐに測定を入手するために有用である。後に行われる測定は血液充満状態に関係する。透明な板材を用いて、予備変調、定常状態の血液量およびより長い期間にわたって平均化された検体測定を得るように、一時的な変調の前および後に生体の組織に接近することが可能である。これらの測定は、変調過程の間において観察される一時的に変化する値を測定するために用いられ得る数を発生する。板材の排除、または板材間または板材の中心への間隙の供与は、板材と相互作用する光を有しない分光的尋問を可能にする。この後者の方法は、板材からの不必要な後方反射による分光計測の汚染を低減する。

#### 【0053】

一実施例において、装置は、連続した輪を形成するように連結された一続きの交互配置の凹所領域および高所領域と、少なくとも1つの回動可能なスプロケットであって前記スプロケットの回動が前記輪の回動をもたらすように前記輪と関係するスプロケットとを含む。凹所領域は平坦または表面にくぼみを有することができる。一実施例において、高所領域は実質的に円筒状または円柱状のローラを含む。ある実施例において、凹所領域は、第1の端部と第2の端部とを有する長さを含む。凹所領域は、さらに、実質的に長方形の断面を有し、実質的に円形の断面を有する部分と一端部で隣接する。

#### 【0054】

一実施例を図8に示す。一連のローラ810とスラット820とはリンク850によって軸860または棒860間に連結されている（ローラは軸を有し、スラットは棒を有する）。これらのローラ810とスラット820とは搬送ベルト型の配列800を構成する。ベルト800は、2つのスプロケット840に取り付けられて折り返されている。スプロケット840は小さなモータによって回されている。ローラ810の動きに関して指の位置と方向付けと温度とを固定する



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板材上に患者は指（または装置に関して適切に配置された他の身体部分）を置くように、装置は位置が合わせられている。

【 0 0 5 5 】

ローラ 810 は、それらは皮膚を押圧する半径から外方へ十分遠く伸びるように、名目上は不透明で円形断面を有する円筒状または円柱状とすることができる。スラットは透明とすることができ、それらはローラで位置を変えるために回りを回転するのでローラと同様に組織をほとんど押圧しない。スラットは、通常の平凸または両凸の断面形状を有する円筒状または円柱状のレンズとして機能する形状とすることができる。ローラの動きは、スラットに関係して組織に対して押圧するとき毛細血管の内外の血液を移動させるものである。スラットの動きは、組織の光への効率的な露出を可能にし、組織からの外方へ散乱する光の効率的な収集を可能にするものである。また、先行するローラによってちょうど圧搾される領域への一時的かつ空間的な正確に規定された接近が生じるために、スラットは光の露出および収集を可能にする。スラットとローラとの合同作動は、血液量とスペクトル測定とを得るように組織を光で同時に調査する間、毛細血管床を反復的に圧搾し緩めることである。

【 0 0 5 6 】

ローラが指を横切って移動するので、血液は周囲の領域に圧搾される。ローラが位置を立ち退くとき、ローラにすぐ追従するスラットは、前に圧搾された領域を再進入する血液の視認を可能にする。スラットは、部分的に光学的に透明または特に選択された光学的フィルタ材料とすることができ、それにより、光が皮膚にすぐに入ることが可能にし、および、露出された領域内からの散乱光が収集され血液量と検体測定とに用いられることを可能にする。また、スラットは、要求された光学的測定に関して有利な形状を有する。一実施例において、スラットは、円筒状または円柱状のレンズとして機能するように形作られる。

【 0 0 5 7 】

他の実施例において、スラットとローラは、組織への圧力がローラの全長軸に沿ってそろわないように形作られる。それゆえ、毛細血管床は、均等には立ち退かされない。補完的な方法において、ローラに追従するスラットの形状は、圧搾

(図1) 102-500908 (P2002-500908A)

および非圧搾された両領域に入るおよびそこから出る光を露出および収集するために形作られる。非圧搾領域がアナログ領域の圧搾領域から自動的に減算されることが可能であるように、収集された光は一本石の空間的に選択的な四分円フォトダイオードまたは分離したアバランシェ フォトダイオードのような光検出器に映写される。これは、毛細血管内の血液流れに関する一時的な情報を同時に得る間において実行されるために、直接のバックグラウンド減算を可能にする。

## 【0058】

いったん先行するローラによって以前に従事される位置にスラットがあると、散乱された青光を観察する信号検出器からの予想値は時間に関する減少関数として現れる。光の減少量は時間が増加するにつれ検出器に近づく。装置は、スラットとローラとの正確かつ速い(50から100 msec)交換を可能にする機械的停止を有する。この信号の一時的な質は、所望の血液検体信号の一時的な質に直接に関係する。このように、位相感知またはゲート型検出は、血液量変調に直接起因する検体信号変調量に用いることができる。これはまた、検出系の取得における増加を可能にして(例えばアバランシェフォトダイオードのような、ただしこれに限定されない)、信号のダイナミック・レンジを効果的に減少させる。

## 【0059】

他の実施例において、分析は、不透明なローラと透明なスラットとの固定的な結合を用いる。この実施例において、透明および不透明領域が所定の位置に機械的に固定されること以外は、装置は前記した装置と実質的に同じである。搬送ベルトは用いない。人は、機械的に固定された組織変調装置に対して組織の圧力を維持する間、親指、指または他の組織領域を結合体に押圧し、それから後方へ引いたりまたは前方へ押したりする。この実施例において、透明な領域は、不透明なローラから生じる領域の調査を可能にする。この変調の時間調整は、患者が指を装置に対していかにすばやく引くまたは押すかによって決定され、変調の増幅は、人が指を装置にいかにしっかり押すかによって決定される。

## 【0060】

他の実施例において、透明なローラと透明なスラットとは用いられる。この実施例の信号標準化はさらに訂正を用いることができる。

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## 【 0 0 6 1 】

本発明の属する技術の分野における通常の知識を有する者は、前記の具体的な実施例に適用することが可能な、かつ本発明の範囲を逸脱しない範囲の、種々の変更や修正を認識することができる。

## 【 図面の簡単な説明 】

## 【 図 1 】

本発明に係る、四分円検出器 1 4 0 との組合せで用いた静的組織変調装置 1 1 0 の一実施例を示す図。

## 【 図 2 】

本発明に係る、四分円検出器 1 4 0 を用いることを示す図。

## 【 図 3 】

本発明に係る組織変調装置 1 1 0 を示し、( A ) は斜視図、( B ) は上面図、( C ) は側面図。

## 【 図 4 】

本発明に係る組織変調装置 1 1 0 の単一の平凸レンズを用いた実施例を示し、( A ) は上面図、( B ) は側面図。

## 【 図 5 】

本発明に係る、偏光ビームスプリッタ 1 2 0 と特定の合焦要素 1 6 0 とが統合された組織変調装置 1 1 0 を示す図。この型の実施例は、1 以上の箇所の同時映写と波長の組合わせの使用とを可能にする。

## 【 図 6 】

本発明に係る、偏光ビームスプリッタ 1 2 0 が統合された組織変調装置 1 1 0 を示す図。

## 【 図 7 】

本発明に係る、組織変調装置 1 1 0 に統合される種々の円筒状のレンズ 7 1 0 から 7 5 0 を示す図。( A ) は装置の長手方向に走る円筒状のレンズ 7 1 0 を示す上面図。( B ) から ( F ) は種々の型の円筒状レンズ 7 1 0 から 7 5 0 を示す側面図。これらの例は、通常の円筒状レンズ 7 1 0、位相シフト／偏光シフトのフィルタ機能を有する断面が四角形のレンズ 7 2 0、断面が三角形のレンズ 7 3

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0、追加合焦要素760との組合せで用いられる通常の円筒状レンズ740、および、スペクトル／偏光／位相フィルタを有し合焦または視準化のための追加要素760との組み合わせで用いられる断面が四角形のレンズ750。

## 【図8】

本発明に係る動的組織変調装置800を示す図で、(A)は一続きのローラ810およびスラット820の側面図、(B)は一続きのローラ810およびスラット820の側面図、(C)は交互に透明領域880を有する不透明領域870があるスラット820の変更を示す側面図。

## 【図9】

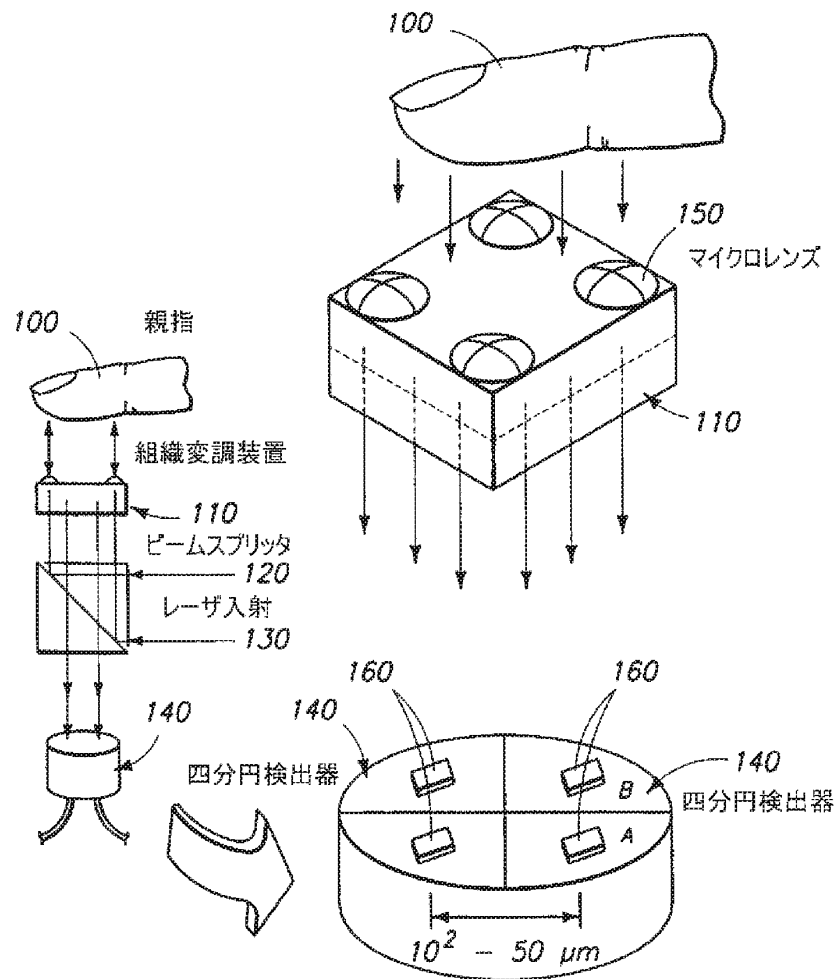
本発明に係る、凹所領域920と変化する高さを有する高所領域910とを特徴とする組織変調装置110の側面図および上面図。「d」は高所領域間の高さの相違を示す。

## 【符号の説明】

- 110 組織変調装置
- 120 ビームスプリッタ
- 140 四分円検出器
- 160 検出器
- 910 高所領域
- 920 凹所領域

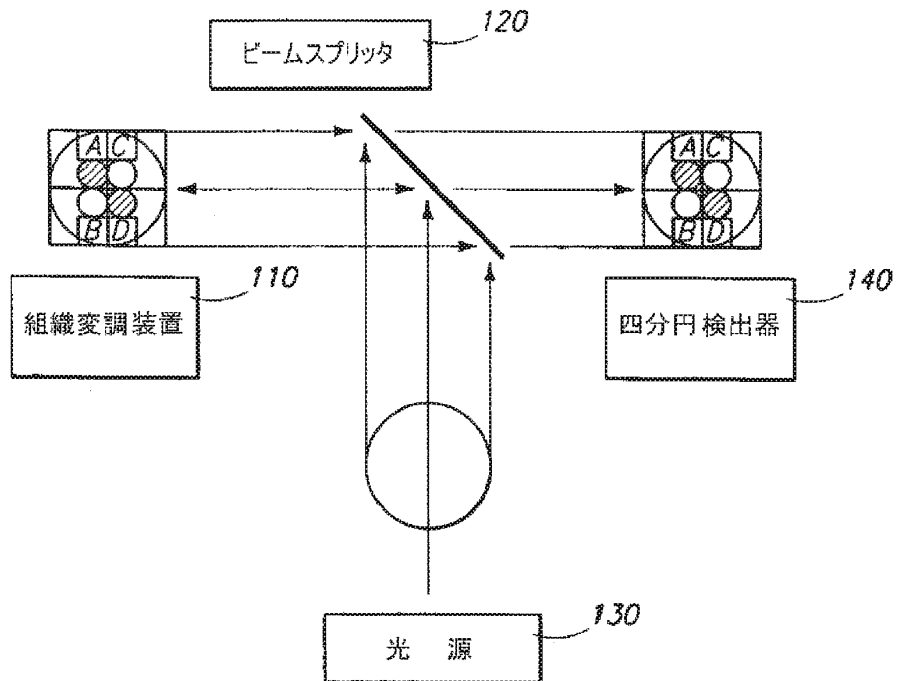
(特4) 102-500908 (P2002-500908A)

【図1】



(特5)102-500908 (P2002-500908A)

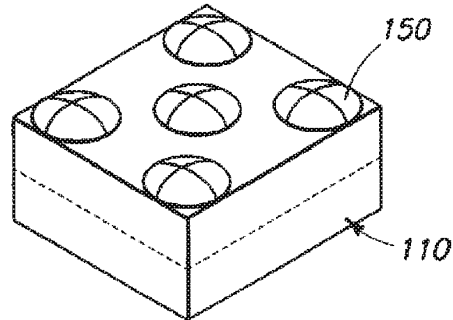
【図2】



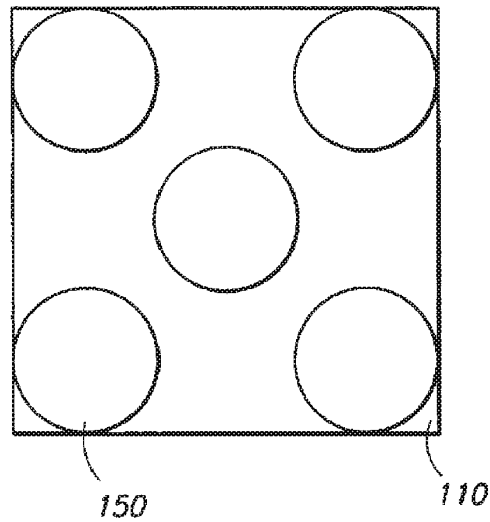
(26) 102-500908 (P2002-500908A)

【図3】

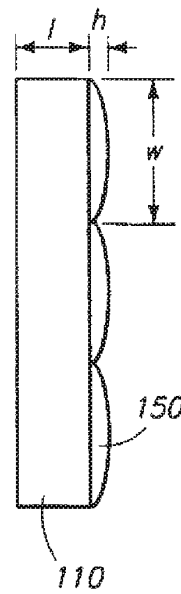
(A)



(B)

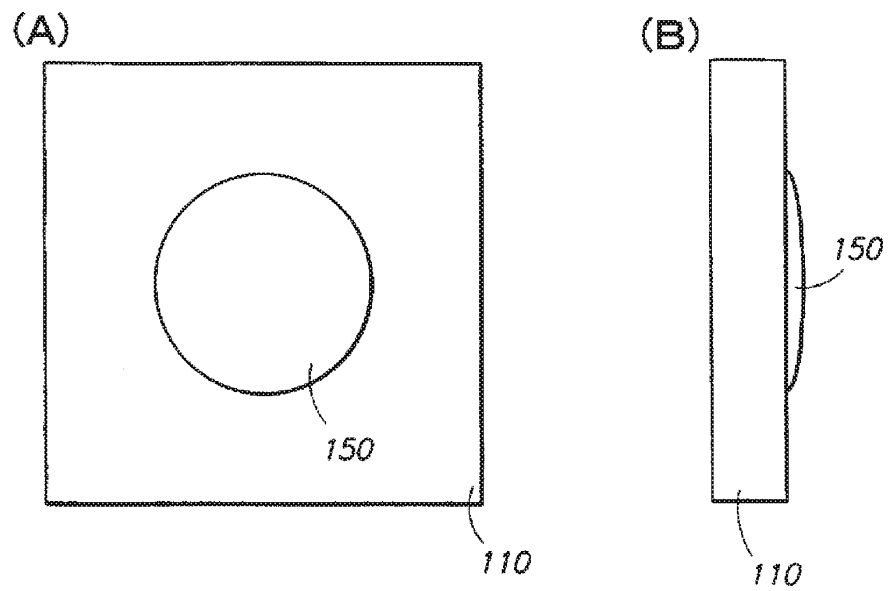


(C)

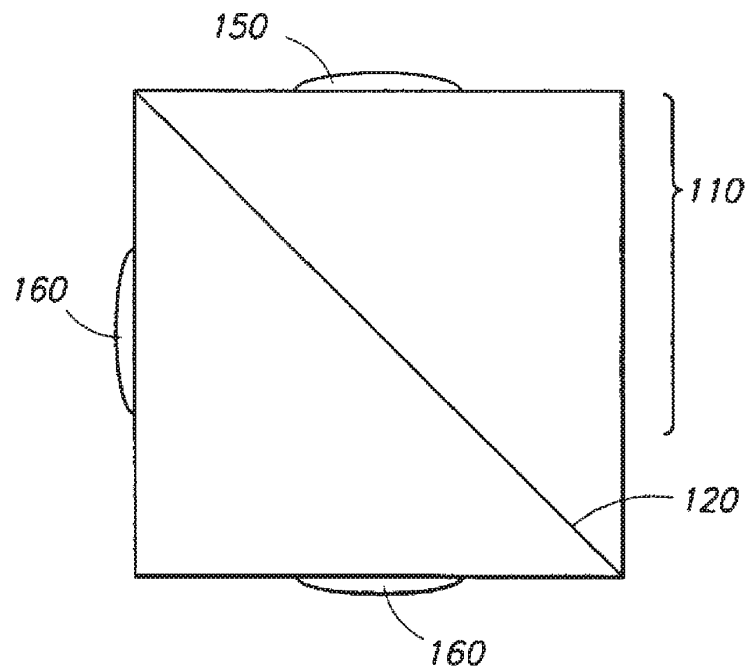


(註7) 102-500908 (P2002-500908A)

【圖4】



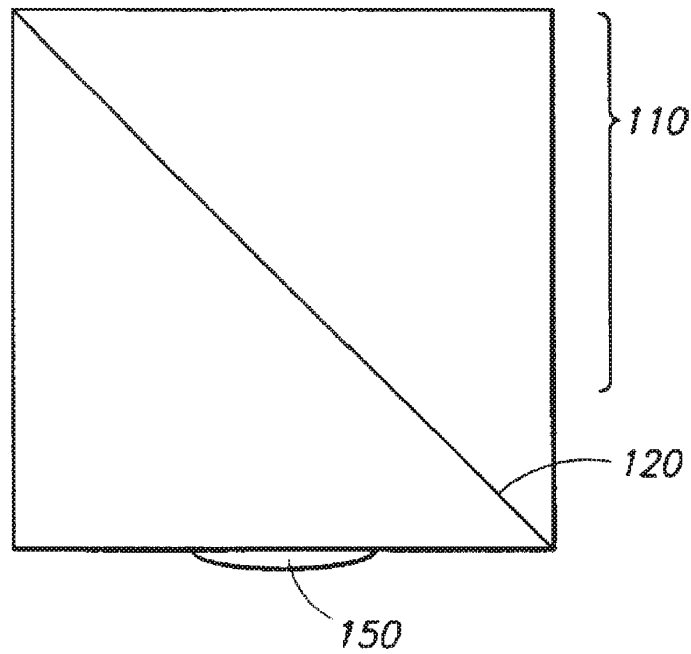
【圖5】





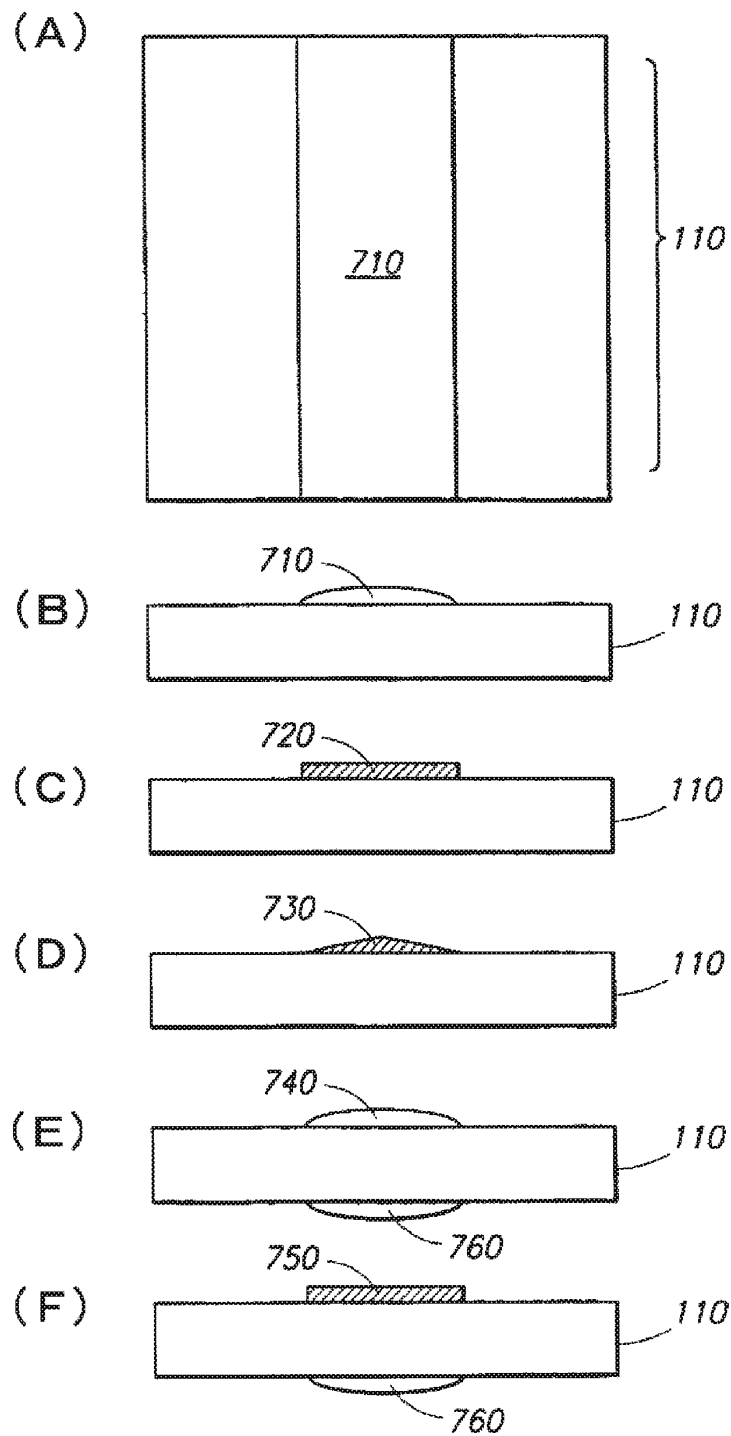
(特許) 102-500908 (P2002-500908A)

【図 6】



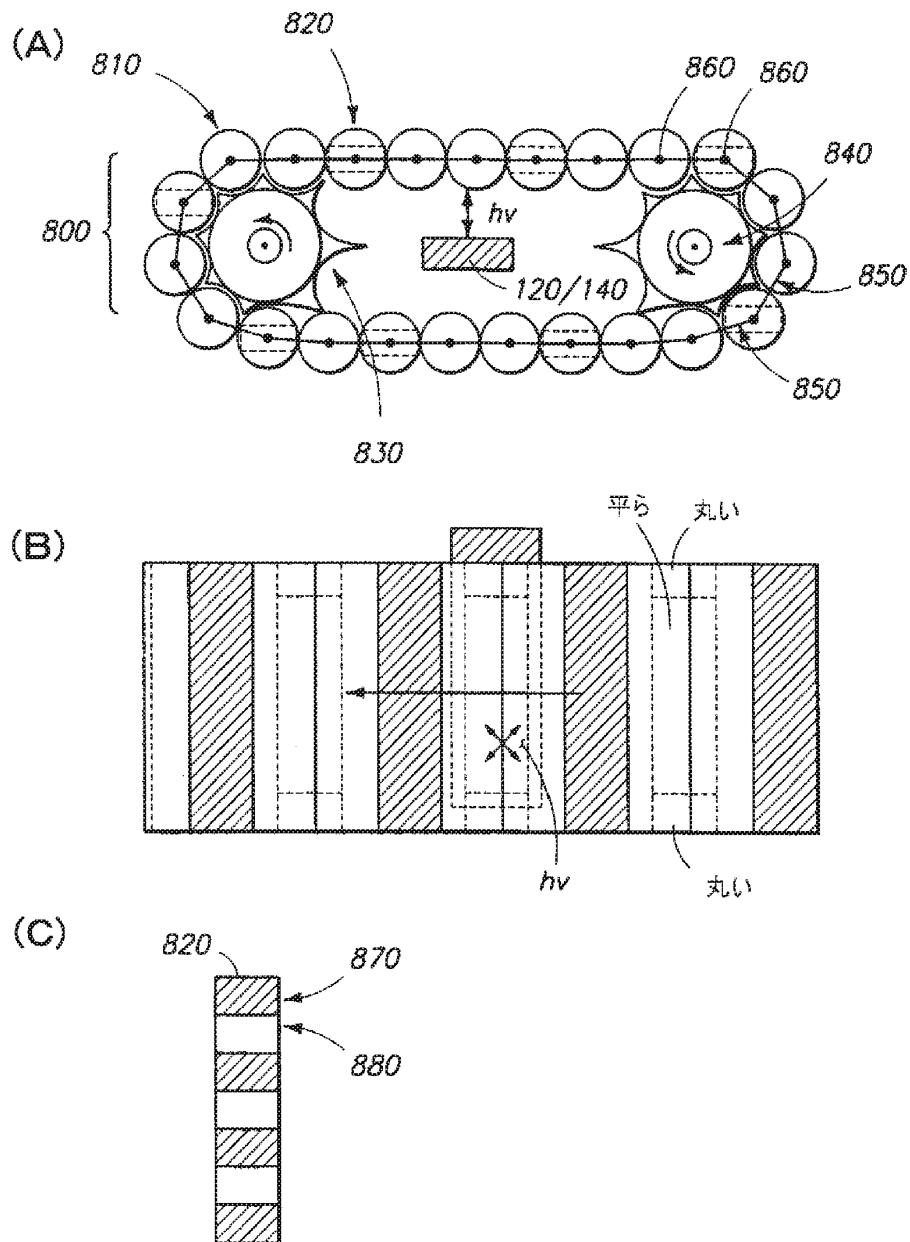
(29) 102-500908 (P2002-500908A)

【 図 7 】



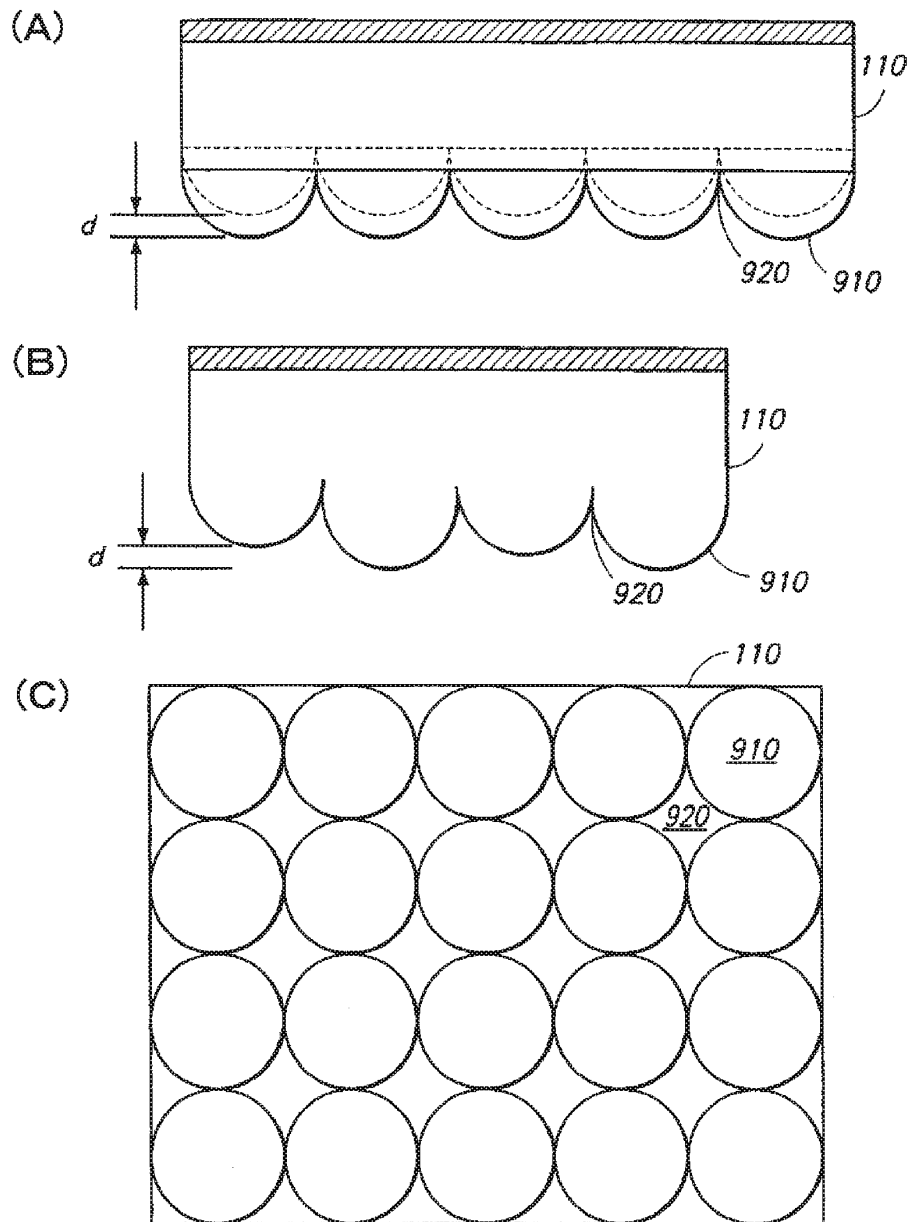
(特) 102-500908 (P2002-500908A)

【図8】



(書1) 02-500908 (P2002-500908A)

【図9】



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(32) 102-500908 (P2002-500908A)

【国際調査報告】

## INTERNATIONAL SEARCH REPORT

International Application No.  
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IPC 6 A61B5/024 A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	see page 35, line 5 - line 13; figure 12	
A	see page 45, line 25 - page 46, line 23	
A	& US 5 551 422 A (J.H. SIMONSEN ET AL.) cited in the application	1,3,4, 14, 18-20,27
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

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"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

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## INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/US 99/01704

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11920

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KA09  
2G059 AA01 BB13 EE03 GG01 JJ02  
JJ22 NN06  
4C038 KK01 KL07 KX01





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**Bibliographic data: JP2007289463 (A) — 2007-11-08**

# BIOLOGICAL INFORMATION MEASURING APPARATUS

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**Classification:** - **international:** A61B5/0245; A61B5/1455  
- **cooperative:** A61B5/6826; A61B5/6838

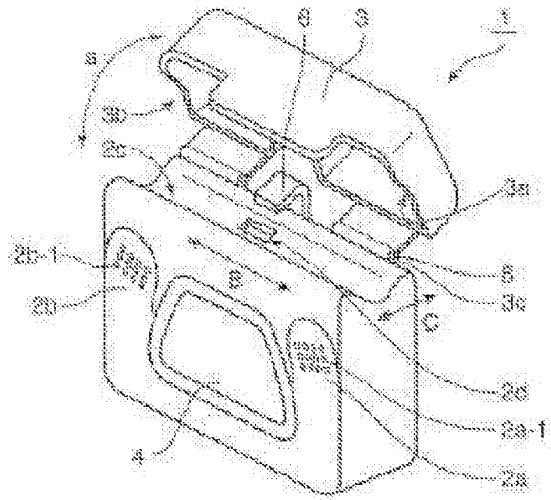
**Application number:** JP20060121588 20060426

**Priority number(s):** JP20060121588 20060426

## Abstract of JP2007289463 (A)

**PROBLEM TO BE SOLVED:** To provide a biological information measuring apparatus which allows to visually confirm a measured result in a stable mounting state even if measurement is performed on either hand finger as a measurement part. **SOLUTION:** A pulse oximeter 1 has a main body part 2 roughly having a plane shape of substantially parallelepiped and having a required thickness and a cover 3 arranged at the upper part of the main body part 2. The main body part 2 includes a display part 4 for displaying the measured result on one side face, has a recessed part 2c extending in left and right directions on the upper surface and has a support shaft 8 extending in the left and right directions at a side end part on the back of the upper surface. The cover 3 has a fitting part 3c to be externally fitted to the support shaft 8 and is configured to be freely turned in a direction indicated by an arrow (a) between an open position at which the recessed part 2c is exposed to the outside and a closing position at which the recessed part 2c is covered with the cover 3. At the respective left and right end parts of the cover 3, notched parts 3a and 3b of a recessed shape are formed. When the cover 3 is positioned at the closing position, a through-hole 9 for fitting the finger is formed of the notched parts 3a and 3b and the recessed part 2c of the main body part 2. **;COPYRIGHT: (C)2008,JPO&INPIT**

CX-1622



(19) 日本国特許庁(JP)

(12) 公開特許公報(A)

(11) 特許出願公開番号

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A61B 5/0245 (2006.01)	A61B 5/02 310D	4C038

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 ニカミノルタセンシング株式会社内  
 Fターム(参考) 4C017 AA09 AA12 AB03 AC27 EE01  
 4C038 KK01 KL05 KL07 KM01 KX01  
 KY01 KY04

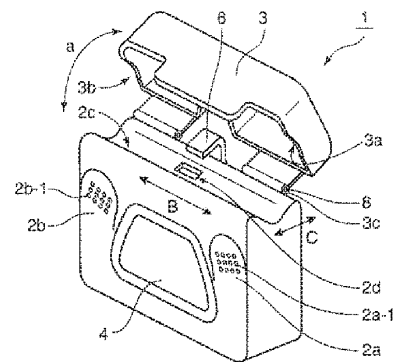
(54) 【発明の名称】 生体情報測定装置

## (57) 【要約】

【課題】どちらの手の指を測定部位として測定する場合であっても、安定した装着状態で測定結果を視認することのできる生体情報測定装置を提供する。

【解決手段】パルスオキシメータ1は、所要の厚みを有する略直方平板形状をする本体部2と本体部2の上部に配置されたカバー3とを有する。本体部2は測定結果を表示するための表示部4を一側面に備え、上面に左右方向に延びる凹部2cを有し、該上面における裏面側端部には左右方向に延びる支持軸8を有する。カバー3は、支持軸8に外嵌する嵌合部3cを有し、凹部2cが外部に露出する開放位置と凹部2cがカバー3により覆われる閉鎖位置との間で矢印a方向に回動自在に構成されている。カバー3の左右各端部には凹形状の切欠き部3a、3bが形成されており、カバー3が閉鎖位置に位置するとき、切り欠き部3a、3bと本体部2の凹部2cとで、指が嵌め込まれる貫通孔9が形成される。

【選択図】 図1



( 2 )

特開2007-289463 (P2007-289463A)

## 【特許請求の範囲】

## 【請求項1】

特定の指を測定部位として所定の生体情報を測定する測定部と、前記測定部により測定される生体情報に由来する生体信号に基づき、生体情報に係るデータを導出する導出部とを内蔵する筐体構造を備え、前記測定指に装着される生体情報測定装置であって、

前記筐体を貫通する貫通孔と、

前記筐体の外壁面に設けられ、前記導出部によって導出された生体情報に係るデータを表示する表示面が前記貫通孔に略沿って形成された表示部とを備え、

前記測定部は、前記貫通孔に挿入された指を測定部位として所定の生体情報を測定することを特徴とする生体情報測定装置。

## 【請求項2】

前記筐体は、本体部と、前記本体部の一侧部に設置されたカバーとを有してなり、

前記貫通孔は、前記本体部と前記カバーとが対向した状態で形成されるものであることを特徴とする請求項1に記載の生体情報測定装置。

## 【請求項3】

前記本体部と前記カバーとの間には、前記貫通孔と略平行な支持軸と、該支持軸と嵌合する嵌合孔とを有する嵌合構造が構成されており、

前記嵌合構造は、前記カバーを前記支持軸を中心として回動可能とすることを特徴とする請求項2に記載の生体情報測定装置。

## 【請求項4】

前記本体部と前記カバーとの間には、前記貫通孔と略平行な支持軸と、該支持軸と嵌合する嵌合孔とを有する嵌合構造が構成されており、

前記嵌合孔は、一方向に長尺の形状を有し、

前記嵌合構造は、前記支持軸が前記嵌合孔内を相対移動することにより、前記カバーを前記本体部に対し対接離反方向に平行移動可能とすることを特徴とする請求項2または3に記載の生体情報測定装置。

## 【請求項5】

前記貫通孔は、該貫通孔に正規の姿勢で指が挿入された状態を想定したとき、該指の腹の部分が反るように、該貫通孔の長手方向に平行な面による切断面が凹形状に形成されていることを特徴とする請求項1ないし4のいずれかに記載の生体情報測定装置。

## 【請求項6】

前記筐体は、略直方形形状を有しており、

前記貫通孔は、前記筐体における外壁面のうち略平行な2の外壁面に交差する面に略沿って形成されており、

前記表示部は、前記2の外壁面のうちいずれか一方の外壁面に設置されていることを特徴とする請求項1ないし5のいずれかに記載の生体情報測定装置。

## 【発明の詳細な説明】

## 【技術分野】

## 【0001】

本発明は、動脈血の酸素飽和度や脈拍数等の生体情報を測定する生体情報測定装置に関する。

## 【背景技術】

## 【0002】

生体組織にとって、酸素は生命活動維持のために最も重要な物質であり、酸素の供給が絶たれると、生体組織細胞は重大なダメージを受けることになるため、臨床において生体組織の酸素濃度を監視する意義は極めて大きい。かかる酸素濃度の監視方法として、生体組織への酸素供給は動脈血によって行われることから、脈拍数や血中酸素飽和度をモニタすることで、生体組織への酸素供給が適切に行われているか否かを把握する手法が一般的に採用されている。従来、動脈血の酸素飽和度等を測定する装置としてパルスオキシメータが知られている。このパルスオキシメータは、被験者の所定の生体部位に装着され、該

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生体部位に向けて光を出力し、生体部位を透過又は反射した光の光量変化をパルス信号として測定し、酸素飽和度を求めるものである。

【0003】

従来のパルスオキシメータは、例えば特許文献1に開示されているように、各種の電気回路、表示部及び所定の指示を入力するためのボタン等が備えられた本体とは別に、酸素飽和度を導出するための検知媒体である光を投受光する発光素子及び受光素子を搭載するプローブが設けられた別体型の装置であったが、近年、例えば図17に示すような一体型のパルスオキシメータが提案されている。

【0004】

図21に示すパルスオキシメータ100は、略直方形形状の本体部101と、該本体部101の上方に位置するカバー102とを備えて構成されている。本体部101の上面における一側端部には、その厚み方向に略平行な支持軸103が形成されており、カバー102は、この支持軸103により回動可能に支持されているとともに、本体部101の上面（図に表れていない）に押し付けられるように、図略のバネ等の付勢部材により付勢されている。また、本体部101の一側面に、測定結果を表示する表示部104が備えられている。

【0005】

そして、酸素飽和度の測定を行う際には、例えば一方の手（図21では右手）の人差し指Fを、前記カバー102に作用する前記付勢力に抗して該カバー102を押し上げて本体部101とカバー102との間に挿入し、該指Fにパルスオキシメータ100を装着するとともに、主に親指と中指とで本体部101を保持する。この状態で、被験者は自らの顔に正対する表示部104にて測定結果を視認する。

【特許文献1】特開平10-314149号公報

【発明の開示】

【発明が解決しようとする課題】

【0006】

しかしながら、前記のような構成を有するパルスオキシメータ100にあつては、右手及び左手のうち一方の手の指にパルスオキシメータ100を装着した場合にしか、容易に表示部104で測定結果を確認することができず、他方の手の指にパルスオキシメータ100を装着した場合には、表示部104が被験者側と反対側に位置することになるため、容易に測定結果を確認することができない。

【0007】

すなわち、図21に示すパルスオキシメータ100においては、右手の指にパルスオキシメータ100を装着したときに表示部104が被験者の顔に正対するが、前記支持軸103の存在により、図22に示すように、左手の指にこのパルスオキシメータ100を装着するときには、パルスオキシメータ100を右手の指に装着する状態から裏返しにする必要があり、このとき、表示部104が被験者の顔に正対せず被験者の顔と反対側（裏側）に位置することとなるため、この場合には、被験者は表示部で測定結果を視認し難くなる。

【0008】

その結果、実質的に測定できる手が制限されることとなり、その手が患者の利き手でない場合には、パルスオキシメータ100が測定指以外の指で保持する必要がある装置であっても、表示部104が被験者の顔と反対側（裏側）に位置した状態では該パルスオキシメータ100を測定指以外の指で確実に保持することができない虞があり、測定精度の低下を招来することとなる。

【0009】

また、一方の手に怪我を負っていて、その手の指にはパルスオキシメータ100を装着できない場合であつて、他方の手の指にパルスオキシメータを装着すると、前記表示部104が被験者の顔と反対側（裏側）に位置することとなった場合には、測定結果の視認動作が不便になる。